PYRIFLUQUINAZON (316)

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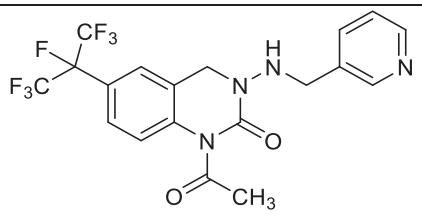
EXPLANATION

Pyrifluquinazon is a quinazinalone insecticide for the control of sap-feeding insects. It acts by modification of insect feeding behaviour. At the Fiftieth Session of the CCPR (2018), it was scheduled for evaluation as a new compound by the 2019 JMPR.

The Meeting received information on the identity, physical and chemical properties, metabolism of pyrifluquinazon in livestock, plants and follow crops, methods of residue analysis, freezer storage stability, GAP information, supervised residue trials on stone fruit (cherries, peaches, plums), potato, tea and tree nuts (almonds, pecans) as well as a livestock feeding study (lactating cow).

IDENTITY

Common name	Pyrifluquinazon
Chemical name IUPAC:	1-acetyl-1,2,3,4-tetrahydro-3-[(3-pyridylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2-one
CAS:	1-acetyl-3,4-dihydro-3-[(3-pyridinylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]-2(1H)-quinazolinone
Manufacturer's code numbers:	NNI-0101
CAS number:	337458-27-2
CIPAC Code:	not allocated
Structural formula:	
Molecular formula:	$C_{19}H_{15}F_7N_4O_2$
Molecular mass:	464.34 g/mol

PHYSICAL AND CHEMICAL PROPERTIES

Specifications for pyrifluquinazon have not been developed by the FAO. Physical and chemical properties of pure pyrifluquinazon and the technical grade pyrifluquinazon are listed in Tables 1 and 2 (pure pyrifluquinazon 99.9% unless stated otherwise).

Table 1 Physical and chemical properties for pyrifluquinazon

Property	Results	Reference
Appearance	White powder	Brands 2005 PC-29007
Melting point	138–139 °C, decomposition starts immediately after melting	Brekelmans 2005 PC-29004 (in Chisholm and Maks 2010 PYF-PRCH-03)
Dissociation constant	No experimental determination was possible. pKa was calculated to be 5.8 in water, from the protonation of the 3-substitued pyridinium group.	Brands 2005 PC-29011 (in Chisholm and Maks 2010 PYF-PRCH-03)
Vapour pressure	5×10^{-8} Pa (4×10^{-10} mm Hg) at 25 °C	Comb 2009 PC-29035 (in Chisholm and Maks 2010 PYF-PRCH-03)

Property	Results	Reference
Volatility	Calculated Henry's law constant at 20 °C: 7.1×10^{-4} kPa m^3/mol	Ikemoto 2013 PC-29045
Solubility in water (at 20 °C)	PAI (99.1%): 0.0121 g/L 1H (IV-01) (98.7%): 5.65 mg/L 1H-imino (IV-02) (99.3%): 0.00811 mg/L	Ikemoto 2003 PC-29006 Yaginuma 2012 PC-29044
Solubility in organic solvents (20 °C)	1,2-dichloromethane ≥ 343 g/L methanol 111 g/L *n*-heptane 0.215 g/L ethyl acetate 170 g/L acetone ≥ 272 g/L xylene 20.2 g/L	Brands 2005 PC-29007
Partition coefficient *n*-octanol/water	PAI (99.1%): log P_{ow} 3.12 at 25 °C	Ikemoto 2005 PC-29008 (in Chisholm and Maks 2010 PYF-PRCH-03)
Partition coefficient *n*-octanol/water of metabolites	At 25 °C the *log* P_{ow} values for the following metabolites were: 1H (IV-01): 3.71 at pH 5.8 1H-imino (IV-02): 4.17 at pH 5.5 1H-4-oxo (IV15): 3.38 at pH 5.7 1H-OH (IV-27): 3.28 at pH 6.3 1H-imino-4-OH (IV-28): 3.64 at pH 5.8 quinazolinedione (IV-203): 3.30 at pH 5.4	Yaginuma 2009 PC-29012
Hydrolysis under sterile conditions (25 °C, dark)	Qn label pH DT_{50} (days) Main degradation products 5 94.9 IV-01 7 23.7 IV-01 9 0.9 IV-01	Lopez 2009 E-29010
	In a separate study at pH 9, DT_{50} = 0.65 days	Hamasaka 2014 E-2902
Photolysis in sterile water	Qn label DT_{50} = 72 days (equivalent solar summer 40 °N latitude) IV-01 was one of the main degradates observed, along with Qn D-1 and Qn D-2	Lopez 2009 E-29011
	Pyr label DT_{50} = 67 days (equivalent solar summer 40 °N latitude) IV-01 was only a minor degradate; the major degradate was IV-402.	Hamasaka 2014 E-29024
	Qn and Pyr label: At 0.005 g/L irradiated with xenon lamp at 25 °C for 4–6 days. Degraded mainly to 1H (IV-01) and minor degradates (<4%) such as 1H-imino (IV-02), 1H-4-oxo (IV-15), 1H-N-Ac (IV-17), N-Ac (IV-101), imino (IV-102), quinazolinedione (IV-203), quinazolinone (IV-206), anthranilic acid (IV-303), anthranilamide (IV-304), and nicotinaldehyde (IV-402).	Ikemoto 2006 E-29002

Table 2 Physical and chemical properties for pyrifluquinazon (technical material, purity 93.0%)

Property	Results	Reference
Appearance	Off white powder	Comb 2009 PC-29034 (in Chisholm and Maks 2010 PYF-PRCH-03)
Odour	No discernible odour	Comb 2009 PC-29034 (in Chisholm and Maks 2010 PYF-PRCH-03)

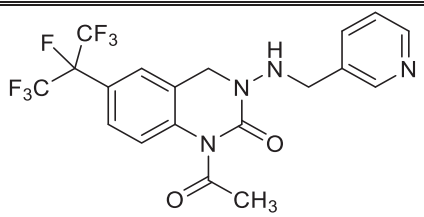
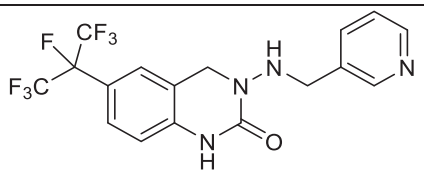
Property	Results	Reference
Relative density	1.523g/cm³ at 20 °C [99.2%]	Comb 2009 PC-29034 (in Chisholm and Maks 2010 PYF-PRCH-03)
pH	TGAI (97%, 1% dispersion): 5.6 ± 0.02 at 20 °C	Comb 2009 PC-29034 (in Chisholm and Maks, 2010 PYF-PRCH-03)
UV/vis light absorption	Neutral methanol 206.4 nm (ε=23297) 214.0 nm (ε=11021)	Comb 2009 PC-29034
Stability	TGAI (97.6%): Chemically stable over 1 year storage period in commercial packaging under normal warehouse conditions.	Comb 2011 PC-29042
Flammability	TGAI (97%): Not a highly flammable solid	Comb 2009 PC-29034 (in Chisholm and Maks 2010 PYF-PRCH-03)
Explosive Properties	TGAI (97%): No explosive properties	Comb 2009 PC-29034 (in Chisholm and Maks 2010 PYF-PRCH-03)
Oxidising Properties	TGAI (97%): No oxidising properties	Comb 2009 PC-29034 (in Chisholm and Maks 2010 PYF-PRCH-03)

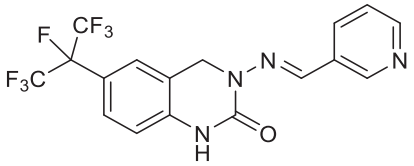
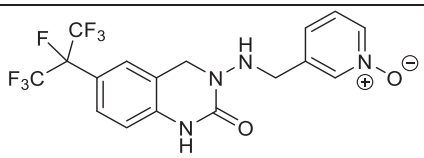
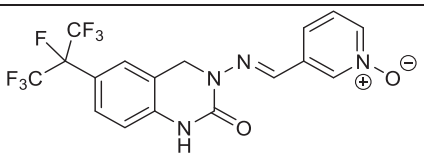
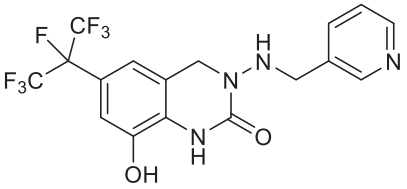
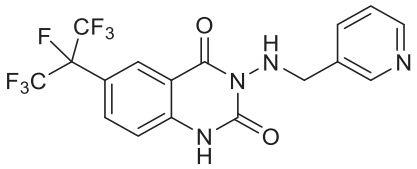
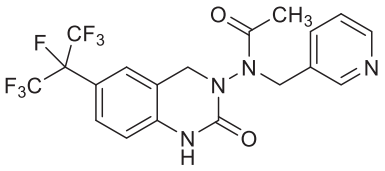
Pyrifluquinazon is applied formulated alone as a 20% w/w suspension concentrate (SC) and 20% w/w water dispersible granule (WG) products.

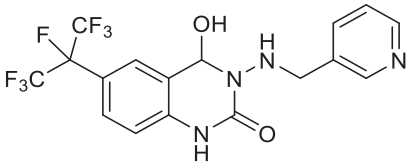
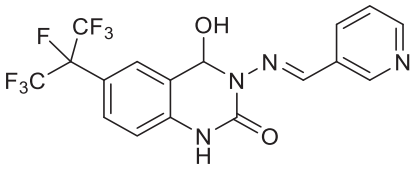
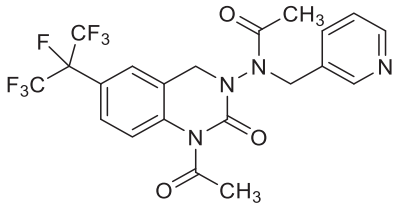
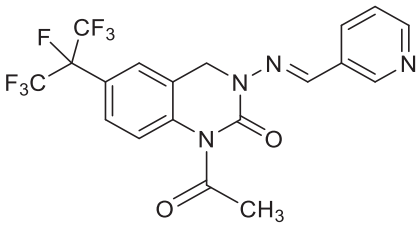
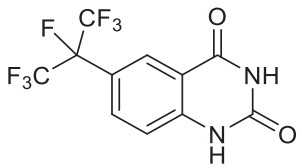
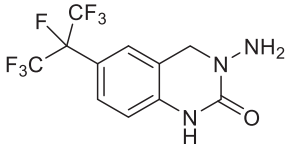
METABOLISM AND ENVIRONMENTAL FATE

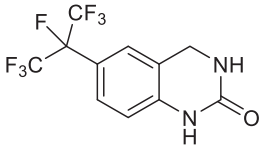
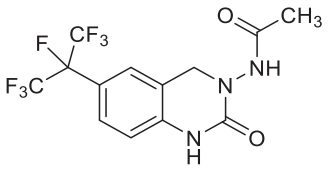
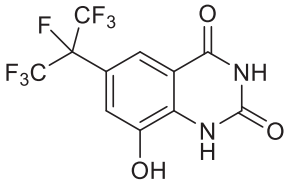
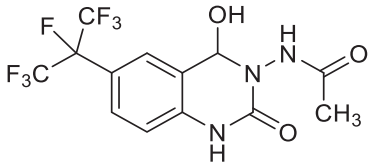
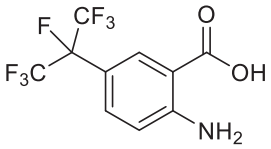
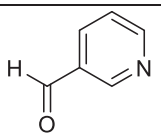
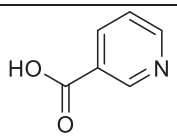
The metabolite summary table provides a reference for the numbering scheme used in the current evaluation (Table 3).

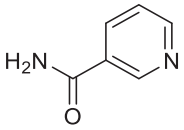
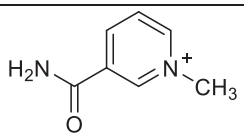
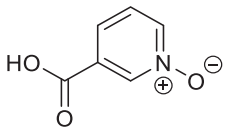
Table 3 Degradation compounds from metabolism of pyrifluquinazon in plants, animals and the environment

Code Names, MW	Chemical Name	Chemical Structure	Where found
Parent Pyrifluquinazon $C_{19}H_{15}F_7N_4O_2$ MW: 464.34 g/mol	1-acetyl-1,2,3,4-tetrahydro-3-[(3-pyridylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2-one		Radish Lettuce Tomato Rat faeces Rat bile
1H (IV-01) $C_{17}H_{13}F_7N_4O$ MW: 422.31 g/mol	1,2,3,4-tetrahydro-3-[(3-pyridylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2-one		Radish Lettuce Tomato Goat kidney Goat liver Goat muscle Goat fat Rat faeces Rat urine and plasma Aerobic soil Anaerobic soil

Code Names, MW	Chemical Name	Chemical Structure	Where found
1H-imino (IV-02) $C_{17}H_{11}F_7N_4O$ MW: 420.29 g/mol	1,2,3,4-tetrahydro-3-[(3-pyridylmethylene)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2-one		Radish Lettuce Tomato Rat faeces Rat plasma and bile Aerobic soil Anaerobic soil
1H-oxide (IV-03) $C_{17}H_{13}F_7N_4O_2$ MW: 438.31 g/mol	1,2,3,4-tetrahydro-3-[3-(1-oxy-pyridylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2-one		Radish Lettuce Tomato Goat kidney Goat liver Goat milk Goat muscle Rat urine Rat plasma Hen liver
1H-imino-oxide (IV-04) $C_{17}H_{11}F_7N_4O_2$ MW: 436.29 g/mol	1,2,3,4-tetrahydro-3-[3-(1-oxy-pyridylmethylene)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2-one		Radish Lettuce Tomato Goat milk Rat urine Rat faeces, plasma and bile
1H-8-OH (IV-09) $C_{17}H_{13}F_7N_4O_2$ MW: 438.31 g/mol	8-hydroxy-3-[(pyridin-3-ylmethyl)amino]-6-[1,2,2,2-tetraftuoro-1-(triftuoromethyl) ethyl]-3,4-dihydro-1H-quinazolin-2-one		Rat faeces
1H-4-oxo (IV-15) $C_{17}H_{11}F_7N_4O_2$ MW: 436.29 g/mol	1,2,3,4-tetrahydro-3-[3-pyridylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2,4-dione		Radish Lettuce Tomato Rotated wheat Hen liver Hen eggs Goat kidney Goat liver Goat milk Aerobic soil
1H-N-Ac (IV-17) $C_{19}H_{15}F_7N_4O_2$ MW: 464.34 g/mol	N-[2-oxo-6-[1,2,2,2-tetrafluoro-1- (trifluoromethyl)ethyl]-1,4-dihydro-2Hquinazolin- 3-yl]-N-(Pyr-3-ylmethyl) acetamide		Radish Lettuce Tomato Goat fat

Code Names, MW	Chemical Name	Chemical Structure	Where found
1H-4-OH (IV-27) (as glucuronide) $C_{17}H_{13}F_7N_4O_2$ MW: 438.31 g/mol	1,2,3,4-tetrahydro-4-hydroxy-3-[3-(pyridylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2-one		Aerobic soil Anaerobic soil Rat bile (Rat bile, faeces)
Metabolite 12 1H-imino-4-OH (IV-28) $C_{17}H_{11}F_7N_4O_2$ MW: 436.29 g/mol	4-hydroxy-3-[(pyridine-3-ylmethylene)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]-3,4-dihydro-1*H*-quinazolin-2-one		Aerobic soil Anaerobic soil
N-AC (IV-101) $C_{21}H_{17}F_7N_4O_3$ MW: 506.38 g/mol	N- [1-acetyl-2-oxo-6- [1,2,2,2-tetrafluoro-1- (trifluoromethyl)ethyl]- 1,4-dihydro-2H- quinazolin-3-yl] -N-(pyridin-3-ylmethyl) acetamide		Radish Lettuce Tomato
imino (IV-102) $C_{19}H_{13}F_7N_4O_2$ MW: 462.33 g/mol	l-acetyl-3- [(pyridin-3-ylmethylene)amino]-6- [1,2,2,2-tetrafluoro- l-(trifluoromethyl)ethyl] -3,4-dihydro-JH-quinazolin-2-one		Radish Lettuce Tomato
quinazolinedione (IV-203) (+conjugate) $C_{11}H_5F_7N_2O_2$ MW: 330.16 g/mol	1,2,3,4-tetrahydro-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2,4-dione		Radish Lettuce Tomato Rotated lettuce Rotated radish Rotated wheat Hen liver Hen eggs Hen muscle Hen fat Goat kidney Goat liver Goat milk Goat muscle Goat fat Rat faeces Rat urine and plasma
Aminoquinazolinone (IV-204) $C_{11}H_8F_7N_3O$ MW: 331.19 g/mol	3-amino-1,2,3,4-tetrahydro-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2-one		Rat plasma

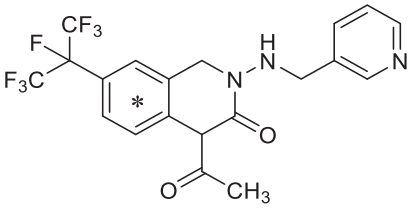
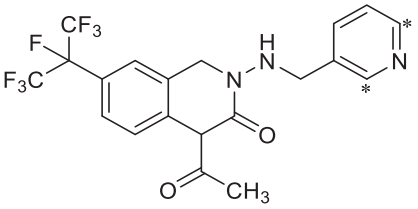
Code Names, MW	Chemical Name	Chemical Structure	Where found
quinazolinone (IV-206) $C_{11}H_7F_7N_2O$ MW: 316.18 g/mol	6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]-3,4-dihydro-lH-quinazolin-2-one		Radish Lettuce Tomato Rat plasma
aminoquinazolinone-N-Ac (IV-208) $C_{13}H_{10}F_7N_3O_2$ MW: 373.23 g/mol	*N*-[2-oxo-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]-1,4-dihydro-2*H*-quinazolin-3-yl]acetamide		Rotated radish foliage Hen liver Hen eggs Hen muscle Hen fat Goat liver Goat kidney Goat muscle Goat fat Goat milk Rat plasma
8-OH-quinazolinedione (IV-211) (as glucuronide) $C_{11}H_5F_7N_2O_3$ MW: 346.16 g/mol	1,2,3,4-tetrahydro-8-hydroxy-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2,4-dione		Goat fat Rat faeces (Rat urine and bile)
aminoquinazolinone-N-Ac-4-OH (IV-212) Conjugate $C_{13}H_{10}F_7N_3O_3$ MW: 389.23 g/mol	*N*-[4-hydroxy-2-oxo-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]-1,4-dihydro-2H-quinazolin-3-yl]acetamide		Rat faeces Rat bile
anthranilic acid (IV-303) $C_{10}H_6F_7NO_2$ MW: 305.15 g/mol	2-amino-5-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]benzoic acid		Hen fat Goat fat Rat faces, urine, plasma and bile
nicotin aldehyde (IV-402) C_6H_5NO MW: 107.11 g/mol	Pyridin-3-aldehyde		Rat blood and liver
Nicotinic acid (IV-403) $C_6H_5NO_2$ MW: 123.11 g/mol	Pyridine-3-carboxylic acid		Hen muscle Goat milk Goat liver Rat faeces, urine, blood, liver, brain, heart

Code Names, MW	Chemical Name	Chemical Structure	Where found
nicotinamide (Niacinamide) (IV-404) $C_6H_6N_2O$ MW: 122.13 g/mol	Pyridine-3-carboxylic acid amide		Hen liver Hen eggs Hen muscle Hen fat Goat liver Goat kidney Goat muscle Goat fat Goat milk Rat urine Rat liver Rat faeces, blood, brain, heart
methyl nicotinamide (IV-405) $C_7H_9N_2O^+$ MW: 137.16 g/mol	3-carbamoyl-1-methylpyridinium		Goat kidney Goat milk Rat urine
nicotinic acid N-oxide $C_6H_5NO_3$ MW: 139.11 g/mol	Nicotinic acid *N*-oxide		Goat milk

* Maximum levels of radioactivity in the matrix are reported as %TRR, apart from soil values which are expressed as %AR (applied radioactivity). Soil values are the maximum observed.

The Meeting received studies on the metabolism of pyrifluquinazon in plants (radish, lettuce and tomato), laboratory animals (rats) as well as lactating goats and laying hens. The metabolism of pyrifluquinazon in plants, animals and soils was investigated using [quinazolinone-phenyl-U-^{14}C]-pyrifluquinazon and [pyridine-2,6-^{14}C]-pyrifluquinazon. The structural formula and the positions of the ^{14}C label are shown below. The studies on laboratory animals were evaluated by the WHO Core Assessment Group.

Table 4 Location of labels in compounds used in metabolism and environmental studies

	
[quinazolinone-phenyl ring-^{14}C(U)] pyrifluquinazon (Qn-label)	[pyridine ring-2,6-^{14}C] pyrifluquinazon (Pyr-label)
Livestock: Goat, poultry	Livestock: Goat, poultry
Plant commodities: Radish, lettuce, tomato	Plant commodities: Radish, lettuce, tomato
Environment: Soil	Environment: Soil

The identification of residue components in the animal and plant metabolism studies was achieved using, where available, authentic standards of the compounds and MS-spectroscopy. There

was little change in metabolite profiles analysed shortly after samples were collected and at the end of the analytical phase suggesting the results of the studies reviewed are representative of the metabolites present.

PLANT METABOLISM

The Meeting received plant metabolism studies with pyrifluquinazon on three different crop groups using foliar application treatments. The crops studied are representative of fruiting vegetables (tomato), leafy vegetables (lettuce), and root and tuber vegetables (radish).

Foliar applications

Tomato

Ikemoto (2006 R-29006) studied the metabolism study for ^{14}C-pyrifluquinazon in cherry tomato (var Chika) labelled at two positions; [quinazolinone-phenyl-^{14}C(U)] pyrifluquinazon and [pyridine ring-2,6-^{14}C] pyrifluquinazon following foliar application of a water dispersible granule formulation (20% w/w) applied three times, with 7-day intervals and at 0.1 kg ai/ha. The plants were maintained in a greenhouse with a quartz ceiling. Fruits and leaves were collected 0, 1, 7 and 14 days after last application (DALA). At 14 DALA stems and roots were also sampled. The surface of the fruit, leaves and stems were rinsed with acetonitrile/water (4:1, v/v). Roots were rinsed with distilled water to remove excess soil. All samples were homogenised and extracted three times with acetonitrile. Post solvent extraction solids (PES) were further sequentially extracted with acetonitrile/0.1N HCl (4:1, v/v), acetonitrile/0.1N NaOH (4:1, v/v) and by hydrolysis with 2N HCl in 1,4-dioxane (100 °C, 2 hours) for lignin solubilisation.

TRR was determined in extracts, rinsates and PES. Identification of constituents was by radio TLC, radio HPLC and LC-MS. Samples were stored frozen (-20 °C) between harvest and analysis. All samples were extracted and metabolite characterisation performed within 6 days of sampling.

The extractability of ^{14}C with acetonitrile was good for fruit (> 71% TRR) and leaves (> 83% TRR) (Tables 5 and 8).

The majority of radioactivity in fruits, leaves and stems was recovered in the surface rinse for both radiolabels (≥ 41% TRR fruit, > 60% TRR leaves).

Table 5 Characterization of TRR in tomato Pyr-label experiment (Ikemoto 2006 R-29006)

	TRR (mg equiv/kg)	Solvent extracted (%TRR)			PES (%TRR)			
		Rinse	ACN	Total	ACN/HCl	ACN/ NaOH	Lignin fraction	Total [a]
Fruit								
0 DALA	0.346	69.87	15.05	84.92	6.85	NA	NA	15.08
1 DALA	0.628	62.70	19.35	82.05	8.15	3.71	NA	17.95
7 DALA	0.411	41	35.26	76.26	6.18	6.87	6.1	23.74
14 DALA	0.65	49.22	22.19	71.41	9.76	4.72	7.79	28.59
Leaves								
0 DALA	13.278	73.49	19.05	92.54	NA	NA	NA	7.46
1 DALA	17.944	80.23	12.79	93.02	NA	NA	NA	6.98
7 DALA	13.523	75.4	18.3	93.7	NA	NA	NA	6.3
14 DALA	13.060	69.14	20.16	89.3	6.51	NA	NA	10.7
Stem								
14 DALA	0.67	67.23	18.23	85.46	5.78	NA	NA	14.54
Root								
14 DALA	0.051	NA	45.33	45.33	12.29	11.73	9.02	54.67

[a] PES total includes radioactivity remaining in solids after additional harsh treatments

Table 6 Characterization of TRR in tomato Qn-label experiment (Ikemoto 2006 R-29006)

	TRR (mg equiv/kg)	Solvent extracted (%TRR)			PES (%TRR)			
		Rinse	ACN	Total	ACN/HCl	ACN/ NaOH	Lignin fraction	Total [a]
Fruit								
0 DALA	0.608	75.23	15.02	90.25	2.94	NA	NA	9.75
1 DALA	0.763	71.7	16.3	88	4.23	NA	NA	12
7 DALA	0.612	68.98	17.05	86.03	2.89	3.66	3.88	13.97
14 DALA	0.514	58.98	20.31	79.29	8.41	4.55	4.84	20.71
Leaves								
0 DALA	14.355	80.22	13.02	93.24	NA	NA	NA	6.76
1 DALA	17.144	72.24	18.84	91.08	NA	NA	NA	8.92
7 DALA	15.98	70.56	17.93	88.49	6.39	NA	NA	11.51
14 DALA	20.665	60.28	23.06	83.34	8.78	NA	NA	16.66
Stem								
14 DALA	1.295	70.13	16.1	86.23	5.43	NA	NA	13.77
Root								
14 DALA	0.160	NA	50.56	50.56	8.15	11.77	11.33	49.44

[a] PES total includes radioactivity remaining in solids after additional harsh treatments

The rinsate and acetonitrile extracts were subjected to radio-TLC and radio-HPLC and the distribution of metabolites in tomato are displayed in Tables 7 and 8.

Table 7 Identification of residues in tomato Pyr-label experiment (Ikemoto 2006 R-29006)

	Fruit				Leaves				Stem	Root
	0 DALA	1 DALA	7 DALA	14 DALA	0 DALA	1 DALA	7 DALA	14 DALA	14 DALA	14 DALA
TRR (mg equiv/kg)	**0.346**	**0.628**	**0.411**	**0.65**	**13.278**	**17.944**	**13.523**	**13.060**	**0.67**	**0.051**
	%TRR									
Solvent extracts (rinsate+ACN)	**84.91**	**82.02**	**76.25**	**71.41**	**92.54**	**93.03**	**93.70**	**89.27**	**85.47**	**45.31**
Pyrifluquinazon	*61.02*	*62.49*	*41.87*	*49.69*	*67.49*	*71.59*	*67.76*	*67.48*	*57.97*	*6.54*
1H (IV-01)	*11.37*	*5.24*	*3.55*	*3.38*	*9.81*	*5.19*	*2.73*	*2.55*	*2.17*	*4.76*
1H-imino (IV-02)	*0.87*	*0.50*	*0.27*	*0.38*	*2.02*	*1.97*	*0.69*	*0.77*	*0.50*	*2.26*
1H-oxide (IV-03)	*0.03*	*0.07*	*ND*	*ND*	*0.14*	*0.25*	*0.05*	*ND*	*0.09*	*ND*
1H-imino-oxide (IV-04)	*0.06*	*ND*	*ND*	*ND*	*0.30*	*0.25*	*0.20*	*0.25*	*ND*	*ND*
1H-4-oxo (IV-15)	*0.76*	*0.56*	*0.70*	*0.81*	*0.96*	*0.95*	*1.01*	*1.36*	*2.39*	*3.02*
1H-N-Ac (IV-17)	*0.75*	*0.53*	*0.30*	*0.38*	*0.78*	*0.44*	*0.09*	*0.08*	*0.11*	*ND*
N-Ac (IV-101)	*0.49*	*0.63*	*0.29*	*0.30*	*0.55*	*0.54*	*0.34*	*0.23*	*0.51*	*ND*
imino (IV-102)	*0.44*	*0.52*	*0.36*	*0.43*	*1.11*	*2.13*	*1.74*	*1.02*	*0.88*	*ND*
Total identified	*75.8*	*70.5*	*47.3*	*55.4*	*83.2*	*83.3*	*74.6*	*73.7*	*64.6*	*16.6*
Others	*6.25 (n=20; max 1.0)*	*7.31 (n=18; max 2.9)*	*15.52 (n=11; max 8.8)*	*10.23 (n=15; max 5.5)*	*4.88 (n=17; max 0.9)*	*4.84 (n=14; max 0.9)*	*4.92 (n=8; max 1.7)*	*8.54 (n=19; max 1.4)*	*10.03*	*1.70*
Origin	*2.88*	*4.16*	*13.39*	*5.82*	*4.49*	*4.86*	*14.16*	*6.99*	*10.82*	*27.04*
PES	**15.09**	**17.98**	**23.75**	**28.59**	**7.46**	**6.97**	**6.30**	**10.73**	**14.53**	**54.69**
ACN/HCl	*6.85*	*8.15*	*6.18*	*9.76*				*6.51*		
ACN/NaOH		*3.71*	*6.87*	*4.72*						

	Fruit				Leaves				Stem	Root
	0 DALA	1 DALA	7 DALA	14 DALA	0 DALA	1 DALA	7 DALA	14 DALA	14 DALA	14 DALA
Lignin fraction			*6.10*	*7.79*						

Table 8 Identification of residues in tomato Qn-label experiment (Ikemoto 2006 R-29006)

	Fruit				Leaves				Stem	Root
	0 DALA	1 DALA	7 DALA	14 DALA	0 DALA	1 DALA	7 DALA	14 DALA	14 DALA	14 DALA
TRR (mg equiv/kg)	**0.608**	**0.763**	**0.612**	**0.514**	**14.355**	**17.144**	**15.98**	**20.665**	**1.295**	**0.16**
	%TRR									
Solvent extracts (rinsate+ACN)	**90.26**	**87.98**	**86.04**	**79.28**	**93.24**	**91.07**	**88.48**	**83.35**	**86.23**	**50.57**
Pyrifluquinazon	*71.51*	*71.82*	*66.79*	*47.65*	*66.91*	*61.31*	*50.44*	*45.49*	*41.68*	*17.42*
1H (IV-01)	*2.40*	*2.39*	*3.19*	*4.38*	*7.88*	*4.92*	*2.26*	*1.10*	*2.03*	*3.34*
1H-imino (IV-02)	*0.35*	*0.29*	*0.21*	*0.43*	*1.45*	*2.06*	*1.24*	*1.37*	*1.06*	*2.96*
1H-oxide (IV-03)	*ND*	*ND*	*0.06*	*ND*	*0.17*	*0.40*	*0.09*	*0.05*	*0.18*	*ND*
1H-imino-oxide (IV-04)	*ND*	*ND*	*ND*	*ND*	*0.28*	*0.28*	*0.42*	*ND*	*0.11*	*ND*
1H-4-oxo (IV-15)	*0.61*	*0.63*	*0.61*	*0.85*	*0.82*	*1.09*	*1.49*	*1.36*	*1.87*	*2.47*
1H-N-Ac (IV-17)	*ND*	*ND*	*ND*	*ND*	*0.18*	*0.14*	*ND*	*ND*	*ND*	*0.28*
N-Ac (IV-101)	*ND*	*ND*	*0.10*	*ND*	*ND*	*ND*	*ND*	*ND*	*ND*	*0.30*
imino (IV-102)	*1.09*	*1.25*	*0.85*	*0.35*	*1.36*	*2.74*	*4.23*	*2.04*	*3.60*	*1.26*
quinazolinedione (IV-203)	*0.31*	*0.25*	*0.43*	*0.63*	*1.33*	*1.00*	*2.33*	*4.50*	*2.91*	*1.66*
quinazolinone (IV-206)	*0.73*	*0.76*	*0.75*	*0.61*	*0.98*	*1.17*	*1.20*	*1.56*	*1.78*	*0.42*
Total identified	*77.0*	*77.4*	*73.0*	*54.9*	*81.4*	*75.1*	*63.7*	*57.5*	*55.2*	*30.1*
Others	*9.24 (n=22; max 2.0)*	*7.62 (n=20; max 1.1)*	*9.49 (n=10; max 4.6)*	*16.97 (n=18; max 9.9)*	*8.15 (n=21; max 1.3)*	*9.95 (n=25; max 1.6)*	*14.76 (n=22; max = 4.0)*	*19.59 (n=23; max 4.2)*	*22.18*	*11.50*
Origin	*4.02*	*2.96*	*3.57*	*7.40*	*3.73*	*6.00*	*10.02*	*6.30*	*8.84*	*8.96*
PES	***9.74***	***12.02***	***13.96***	***20.72***	***6.76***	***8.93***	***11.52***	***16.65***		
ACN/HCl	*2.94*	*4.23*	*2.89*	*8.41*			*6.39*	*8.78*		
ACN/NaOH			*3.66*	*4.55*						
Lignin fraction			*3.88*	*4.84*						

Parent pyrifluquinazon was the major component observed in all fruit and leaf samples (Pyr-label 41.9–62.5% TRR fruit, 67.5–71.6% TRR leaves; Qn-label 47.7–71.8% TRR fruit, 45.5–66.9% TRR leaves). Major metabolites were 1H (IV-01) (Pyr-label fruit 3.4–11.4% TRR, leaves 2.6–9.8% TRR; Qn-label fruit 2.4–4.4% TRR, leaves 1.1-7.9% TRR).

Further metabolites were detected at low levels (<10% TRR) included; lH-imino (IV-02), lH-oxide (IV-03), lH-imino-oxide (IV-04), lH-4-oxo (IV-15), 1H-N-Ac (IV-17), N-Ac (IV-101), imino (IV-102), quinazolinedione (IV-203) and quinazolinone (IV-206). Several minor unidentified metabolites were observed in each sample however, no unidentified metabolite exceeded 10% TRR and 0.01 mg eq/kg.

A portion of the ^{14}C in fruit was associated with lignin (3.9–7.8% TRR).

The metabolism of pyrifluquinazon in/on tomato proceeds predominately through deacetylation of the quinazolinone nitrogen forming 1H (IV-01) and dehydrogenation to imino (IV-102), which may be hydrolysed to the deacetylated metabolite, 1H-imino (IV-02). A small portion of radioactivity is incorporated into natural products (lignin).

Lettuce

Ikemoto 2006 (R-29002) studied the uptake and metabolism of [pyridine-2,(6)-^{14}C]– or [quinazolinone-phenyl-U-^{14}C]-pyrifluquinazon applied in a WG formulation to lettuce plants (variety: Cisco – head lettuce) as three foliar applications at seven day intervals, each at an application rate of 0.2 kg ai/ha. The plants were maintained in a greenhouse with a quartz ceiling. Lettuce heads and outer leaves were collected 0, 1, 7 and 14 days after last application. At 14 DALA stems and roots were also sampled. The surface of the heads and leaves were rinsed with acetonitrile/water (4:1, v/v). Roots were rinsed with distilled water to remove excess soil. All samples were homogenised and extracted three times with acetonitrile. PES were further sequentially extracted with acetonitrile/0.1N HCl (4:1, v/v), acetonitrile/0.1N NaOH (4:1, v/v) and by hydrolysis with 2N HCl in 1,4-dioxane (100 °C, 1 hour) for lignin solubilisation.

TRR was determined in extracts, rinsates and PES. Identification of constituents was by radio TLC, radio HPLC and LC-MS. Samples were stored frozen (-20 °C) between harvest and analysis. The interval between harvest and initial analysis by TLC was 51–70 days.

The extractability of ^{14}C with acetonitrile was good for lettuce leaf (> 89% TRR) and quite good for stems (> 62% TRR) (Tables 9 and 10).

The majority of radioactivity was recovered in the leaf rinse and acetonitrile extracts for both radiolabels with little translocation to roots.

Table 9 Characterization of TRR in lettuce Pyr-label experiment (Ikemoto 2006 R-29002)

	TRR	Solvent extracted (%TRR)			PES (%TRR)			
	(mg equiv/kg)	Rinse	ACN	Total	ACN/HCl	ACN/ NaOH	Lignin fraction	Total [a]
Head								
0 DALA	1.821	81.92	14.47	96.39	NA	NA	NA	3.61
1 DALA	2.323	87.69	7.37	95.06	NA	NA	NA	4.94
7 DALA	0.867	92.54	4.17	96.71	NA	NA	NA	3.29
14 DALA	0.568	60.97	28.84	89.81	3.79	NA	NA	10.19
Outer leaves								
0 DALA	19.167	78.44	14.83	93.27	NA	NA	NA	6.73
1 DALA	24.037	81.03	10.38	91.41	NA	NA	NA	8.59
7 DALA	17.216	71.86	17.58	89.44	2.98	NA	NA	10.56
14 DALA	16.848	84.91	4.92	89.83	2.09	NA	NA	10.17
Stem								
14 DALA	0.233	NA	62.71	62.71	11.45	3.88	2.22	37.29
Root								
14 DALA	0.063	NA	33.78	33.78	8.77	5.95	20.37	66.22

[a] PES total includes radioactivity remaining in solids after additional harsh treatments

Table 10 Characterisation of TRR in lettuce Qn-label experiment (Ikemoto 2006 R-29002)

	TRR	Solvent extracted (%TRR)			PES (%TRR)			
	(mg equiv/kg)	Rinse	ACN	Total	ACN/HCl	ACN/ NaOH	Lignin fraction	Total [a]
Head								
0 DALA	2.927	89.2	8.53	97.73	NA	NA	NA	2.27
1 DALA	0.59	89.2	6.86	96.06	NA	NA	NA	3.94
7 DALA	0.555	81.6	13.82	95.42	NA	NA	NA	4.58
14 DALA	1.419	77.2	19.01	96.21	NA	NA	NA	3.79
Outer leaves								

	TRR (mg equiv/kg)	Solvent extracted (%TRR)			PES (%TRR)			
		Rinse	ACN	Total	ACN/HCl	ACN/ NaOH	Lignin fraction	Total [a]
0 DALA	21.372	47.53	43.79	91.32	NA	NA	NA	8.68
1 DALA	23.740	83.24	11.06	94.3	NA	NA	NA	5.7
7 DALA	24.910	83	12.05	95.05	NA	NA	NA	4.95
14 DALA	24.067	87.48	6.76	92.24	NA	NA	NA	5.76
Stem								
14 DALA	0.304	NA	80.77	80.77	6.82	2.45	NA	19.23
Root								
14 DALA	0.103	NA	23.10	23.10	6.42	6.20	7.62	76.9

[a] PES total includes radioactivity remaining in solids after additional harsh treatments, i.e. 100-%Total solvent extracted

The leaf rinse and acetonitrile extracts were analysed by TLC and HPLC and the distribution of metabolites in lettuce are shown in Tables 11 and 12.

Table 11 Identification of residues in lettuce Pyr-label experiment (Ikemoto 2006 R-29002)

	Heads				Outer leaves				Stem	Root
	0 DALA	1 DALA	7 DALA	14 DALA	0 DALA	1 DALA	7 DALA	14 DALA	14 DALA	14 DALA
TRR (mg equiv/kg)	**1.821**	**2.323**	**0.867**	**0.568**	**19.167**	**24.037**	**17.216**	**16.848**	**0.233**	**0.063**
%TRR										
Solvent extracts (rinsate+ACN)	**96.39**	**95.06**	**96.81**	**89.81**	**93.27**	**91.41**	**89.44**	**89.83**	**62.71**	**33.78**
Pyrifluquinazon	*10.01*	*10.65*	*3.02*	*12.14*	*77.15*	*80.02*	*71.43*	*71.70*	*4.21*	*2.48*
1H (IV-01)	*79.37*	*76.87*	*81.63*	*59.74*	*6.64*	*2.38*	*6.59*	*10.51*	*14.53*	*9.38*
1H-imino (IV-02)	*2.27*	*1.22*	*1.17*	*3.82*	*0.54*	*0.37*	*0.53*	*0.84*	*5.36*	*5.10*
1H-oxide (IV-03)	*ND*	*0.07*	*ND*	*0.08*	*0.14*	*ND*	*ND*	*ND*	*ND*	*ND*
1H-imino-oxide (IV-04)	*ND*	*ND*	*ND*	*0.27*	*ND*	*ND*	*0.02*	*0.02*	*4.71*	*ND*
1H-4-oxo (IV-15)	*0.36*	*0.48*	*1.78*	*2.48*	*0.34*	*0.44*	*0.64*	*0.51*	*2.31*	*ND*
1H-N-Ac (IV-17)	*1.13*	*1.10*	*0.64*	*0.95*	*0.29*	*0.15*	*0.23*	*0.31*	*ND*	*ND*
N-Ac (IV-101)	*0.03*	*0.02*	*ND*	*ND*	*0.32*	*0.32*	*0.28*	*0.36*	*ND*	*ND*
imino (IV-102)	*0.07*	*0.04*	*ND*	*ND*	*0.44*	*0.74*	*0.43*	*0.29*	*ND*	*ND*
Total identified	*93.2*	*90.5*	*88.2*	*79.5*	*85.9*	*84.4*	*80.2*	*84.5*	*31.1*	*16.96*
Others	*0.90 (n=5; max 0.5)*	*3.20 (n=6; max 2.2)*	*4.76 (n=8; max 1.3)*	*4.33 (n=5; max 2.0)*	*2.96 (n=10; max 1.4)*	*4.35 (n=14; max 1.4)*	*7.13 (n=16; max 3.1)*	*2.97 (n=12; max 1.4)*	*19.27*	*2.59*
Origin	*2.16*	*1.42*	*3.83*	*6.00*	*4.45*	*2.64*	*2.14*	*2.34*	*12.31*	*14.23*
PES	**3.61**	**4.94**	**3.19**	**10.19**	**6.73**	**8.59**	**10.58**	**10.16**	**37.29**	**66.22**
ACN/HCl				*3.79*			*2.98*	*2.09*	*11.45*	*8.77*
ACN/NaOH									*3.88*	*5.95*
Lignin fraction									*2.22*	*20.37*

Table 12 Identification of residues in lettuce Qn-label experiment (Ikemoto 2006 R-29002)

	Heads				Outer leaves				Stem	Root
	0 DALA	1 DALA	7 DALA	14 DALA	0 DALA	1 DALA	7 DALA	14 DALA	14 DALA	14 DALA
TRR (mg equiv/kg)	2.927	0.590	0.555	1.419	21.372	23.740	24.910	24.067	0.304	0.103
%TRR										
Solvent extracts (rinsate+ACN)	**97.73**	**96.06**	**95.41**	**96.21**	**91.32**	**94.30**	**95.05**	**94.24**	**80.77**	**23.10**
Pyrifluquinazon	*71.33*	*12.52*	*7.76*	*12.28*	*80.98*	*81.75*	*73.77*	*64.62*	*29.17*	*0.40*

	Heads				Outer leaves				Stem	Root
	0 DALA	1 DALA	7 DALA	14 DALA	0 DALA	1 DALA	7 DALA	14 DALA	14 DALA	14 DALA
1H (IV-01)	*12.95*	*76.80*	*78.32*	*69.70*	*2.26*	*5.10*	*12.32*	*20.82*	*15.56*	*5.67*
1H-imino (IV-02)	*1.05*	*1.19*	*3.79*	*3.58*	*0.26*	*0.57*	*0.69*	*0.82*	*1.65*	*3.54*
1H-oxide (IV-03)	*ND*	*0.11*	*0.13*	*ND*	*ND*	*ND*	*ND*	*ND*	*ND*	*ND*
1H-imino-oxide (IV-04)	*ND*	*ND*	*ND*	*ND*	*ND*	*ND*	*ND*	*0.02*	*ND*	*0.71*
1H-4-oxo (IV-15)	*0.03*	*0.46*	*0.58*	*0.68*	*0.22*	*0.37*	*0.32*	*0.49*	*0.97*	*1.11*
1H-N-Ac (IV-17)	*ND*	*1.17*	*0.64*	*0.96*	*0.07*	*0.07*	*0.25*	*0.36*	*0.25*	*0.30*
N-Ac (IV-101)	*0.15*	*ND*	*ND*	*0.03*	*0.16*	*0.19*	*0.16*	*0.11*	*ND*	*ND*
imino (IV-102)	*0.19*	*ND*	*ND*	*0.07*	*0.46*	*0.33*	*0.36*	*0.23*	*ND*	*ND*
quinazolinedione (IV-203)	*0.04*	*0.19*	*0.52*	*0.51*	*0.16*	*0.26*	*0.22*	*0.48*	*1.61*	*ND*
quinazolinone (IV-206)	*0.03*	*0.12*	*0.35*	*0.26*	*0.15*	*0.10*	*0.22*	*0.22*	*0.36*	*ND*
Total identified	*85.8*	*92.6*	*92.1*	*88.1*	*84.7*	*88.7*	*88.3*	*88.2*	*49.6*	*11.7*
Others	*5.86 (n=12; max 4.8)*	*2.94 (n=5; max 2.3)*	*1.79 (n=5: max 0.9)*	*5.09 (n=9;max 2.9)*	*4.46 (n=13; max 1.6)*	*3.84 (n=18; max 1.0)*	*4.95 (n=16; max 1.9)*	*4.55 (n=21; max 0.7)*	*27.04*	*6.81*
Origin	*6.10*	*0.58*	*1.52*	*3.06*	*2.15*	*1.73*	*1.80*	*1.54*	*4.16*	*4.56*
PES	**2.27**	**3.94**	**4.58**	**3.78**	**8.68**	**5.70**	**4.95**	**5.76**	**19.23**	**76.90**
ACN/HCl									*6.82*	*6.42*
ACN/NaOH									*2.45*	*6.20*
Lignin fraction										*7.62*

Parent pyrifluquinazon was the major component outer leaves (Pyr-label 64.6–81.8% TRR, Qn-label 71.4–80.0% TRR) and a significant component in heads (Pyr-label 7.8–71.3% TRR; Qn-label 3.0–12.1% TRR). The major metabolite was 1H (IV-01); Pyr-label 13.0–78.3% TRR heads, 2.3–20.8% TRR outer leaves; Qn-label 59.7–81.6% TRR heads, 2.4–10.5% TRR outer leaves).

Further metabolites detected at low levels (< 10% TRR) were lH-imino (IV-02), lH-oxide (IV-03), lH-imino-oxide (IV-04), lH-4-oxo (IV-15), 1H-N-Ac (IV-17), N-Ac (IV-101), quinazolinedione (IV-203), quinazolinone (IV-206) and imino (IV-102). Several minor unidentified metabolites were observed in each sample, however no unidentified metabolite exceeded 10% TRR and 0.01 mg eq/kg.

A proportion of the radioactivity in stems and roots for both labels was associated with lignin fractions (2.2–20.4% TRR).

Radioactivity of the TLC origin for the stems and roots at 14 DALA exceeded 10% TRR, however, this seemed to consist of several highly polar metabolites that did not separate despite further TLC analysis using a polar solvent system.

In summary, the main metabolism of pyrifluquinazon in/on lettuce proceeds predominately through the same process as occurs for tomato, that is deacetylation of the quinazolinone nitrogen forming 1H (IV-01) and dehydrogenation to imino (IV-102), which may be hydrolysed to the deacetylated metabolite, 1H-imino (IV-02). Trace amounts of IH-N-Ac (IV-17) and N-Ac (IV-101) were detected resulting from intra and inter molecular trans-acetylation of pyrifluquinazon.

Radish

In a separate study Ikemoto (2006 R-29001) investigated the metabolism of [^{14}C]-pyrifluquinazon on radish plants (variety Cherry Mate) maintained in a greenhouse under a quartz ceiling. Pyr- or Qn–label pyrifluquinazon was applied three times by foliar application of an WG-formulation at seven day intervals and an application rate of 0.1 kg ai/ha. Leaves and roots were collected 0, 1, 7 and 14 days after the final application. Leaves were rinsed with acetonitrile/water (4:1, v/v). Rinsed leaves and

unrinsed roots were homogenised and extracted three times with acetonitrile. PES were further sequentially extracted with acetonitrile/0.1N HCl (4:1, v/v), acetonitrile/0.1N NaOH (4:1, v/v) and by hydrolysis with 2N HCl in 1,4-dioxane (100 °C, 1 hour) for lignin solubilisation. TRR was determined in extracts, rinsates and PES. Identification of constituents was by radio TLC, radio HPLC and LC-MS. Samples were stored frozen (-20 °C) between harvest and analysis. All samples were extracted and metabolite characterisation performed within 71 days of sampling. The interval between harvest and initial analysis by TLC was 41–71 days.

The extractability of ^{14}C with acetonitrile was good for radish leaf (> 75% TRR) and lower for radish root (> 36% TRR) (Tables 13 and 14).

The majority of radioactivity was recovered in the leaf rinse and acetonitrile extracts for both radiolabels. Radioactivity in roots was about 100 times lower than those in leaves. Most of the radioactivity was located in the surface rinse (> 50% TRR) with little translocation to roots. Radioactivity concentrations in leaves and roots decreased with time after application.

Table 13 Characterization of TRR in radish Pyr-label experiment (Ikemoto 2006 R-29001)

	TRR	Solvent extracted (%TRR)			PES (%TRR)			
	(mg equiv/kg)	Rinse	ACN	Total	ACN/HCl	ACN/NaOH	Lignin fraction	Total [a]
Leaves								
0 DALA	10.75	66.39	21.12	87.51	2.79	1.23	1.83	12.49
1 DALA	10.896	64.11	21.54	85.65	3.04	2.17	2.8	14.35
7 DALA	5.844	57.94	17.83	75.77	5.72	1.64	3.01	24.23
14 DALA	3.641	60.36	16.98	77.34	3.98	1.57	4.10	22.66
Roots								
0 DALA	0.158		66.83	66.83	10.14	5.04	7.54	33.17
1 DALA	0.174		53.58	53.58	12.04	9.38	11.88	46.42
7 DALA	0.128		55.96	55.96	20.06	6.59	6.62	44.04
14 DALA	0.076		36.49	36.49	31.43	6.72	8.33	63.51

[a] PES total includes radioactivity remaining in solids after additional harsh treatments

Table 14 Characterization of TRR in radish Qn-label experiment (Ikemoto 2006 R-29001)

	TRR	Solvent extracted (%TRR)			PES (%TRR)			
	(mg equiv/kg)	Rinse	ACN	Total	ACN/HCl	ACN/NaOH	Lignin fraction	Total [a]
Leaves								
0 DALA	14.382	57.56	22.83	80.39	2.33	1.76	3.3	19.61
1 DALA	14.798	50.73	31.84	82.57	2.64	1.62	2.88	17.43
7 DALA	10.933	58.43	17.85	76.28	4.19	2.39	5.44	23.72
14 DALA	5.856	71.90	13.92	85.82	2.30	1.17	3.27	14.18
Roots								
0 DALA	0.113		74.09	74.09	5.77	4.34	4.21	25.91
1 DALA	0.128		68.11	68.11	6.28	5.3	6.3	31.89
7 DALA	0.094		49.12	49.12	13.19	7.81	9.47	50.88
14 DALA	0.058		42.56	42.56	12.46	7.62	10.81	57.44

[a] PES total includes radioactivity remaining in solids after additional harsh treatments

The leaf rinse and acetonitrile extracts from leaves and roots were subjected to TLC and HPLC (Tables 15 and 16).

Table 15 Identification of residues in radish Pyr-label experiment (Ikemoto 2006 R-29001)

	Leaves				Roots			
Component	0 DALA	1 DALA	7 DALA	14 DALA	0 DALA	1 DALA	7 DALA	14 DALA
TRR (mg equiv/kg)	**10.750**	**10.896**	**5.844**	**3.641**	**0.158**	**0.174**	**0.128**	**0.076**
	%TRR							
Solvent extracts (rinsate+ACN)	**87.51**	**85.66**	**75.75**	**77.34**	**66.83**	**53.59**	**55.96**	**36.49**
Pyrifluquinazon	*63.93*	*61.64*	*55.72*	*59.1*	*31.35*	*24.69*	*21.58*	*9.21*
1H (IV-01)	*13.77*	*10.87*	*3.49*	*1.95*	*16.95*	*10.3*	*7.31*	*4.09*
1H-imino (IV-02)	*1.21*	*1.44*	*1.61*	*0.55*	*1.81*	*2.51*	*0.93*	*1.00*
1H-oxide (IV-03)	*1.49*	*2.81*	*2.71*	*1.93*	*ND*	*ND*	*ND*	*ND*
1H-imino-oxide (IV-04)	*ND*	*0.07*	*0.21*	*0.31*	*ND*	*ND*	*ND*	*ND*
1H-4-oxo (IV-15)	*0.52*	*0.45*	*0.64*	*0.66*	*1.18*	*1.34*	*0.76*	*1.12*
1H-N-Ac (IV-17)	*0.57*	*0.53*	*0.19*	*0.05*	*0.36*	*0.47*	*ND*	*ND*
N-Ac (IV-101)	*0.31*	*0.63*	*0.37*	*0.3*	*0.21*	*0.10*	*ND*	*ND*
imino (IV-102)	*0.33*	*0.26*	*0.34*	*0.46*	*0.06*	*0.13*	*ND*	*ND*
Total identified	*82.1*	*78.7*	*65.3*	*65.3*	*51.9*	*39.5*	*30.6*	*15.4*
Others	*3.12 (n=13: max 0.5)*	*4.16 (n=15; max 1.1)*	*5.2 (n=18; max 2.0)*	*4.79 (n=17; max 1.4)*	*8.00 (n=7; max 2.3)*	*9.11 (n=5; max 3.6)*	*9.09 (n=4; max 4.3)*	*5.26 (n=1; max 5.26)*
Origin	*2.25*	*2.80*	*5.28*	*7.25*	*6.91*	*4.93*	*16.29*	*15.82*
PES	**12.49**	**14.34**	**24.25**	**22.66**	**33.17**	**46.41**	**44.04**	**63.51**
ACN/HCl	*2.79*	*3.04*	*5.72*	*3.98*	*10.14*	*12.04*	*20.06*	*31.43*
ACN/NaOH	*1.23*	*2.17*	*1.64*	*1.57*	*5.04*	*9.38*	*6.59*	*6.72*
Lignin fraction	*1.83*	*2.80*	*3.01*	*4.1*	*7.54*	*11.88*	*6.62*	*8.33*

Table 16 Identification of residues in radish Qn-label experiment (Ikemoto 2006 R-29001)

	Leaves				Roots			
Component	0 DALA	1 DALA	7 DALA	14 DALA	0 DALA	1 DALA	7 DALA	14 DALA
TRR (mg equiv/kg)	**14.382**	**14.798**	**10.933**	**5.856**	**0.113**	**0.128**	**0.094**	**0.058**
	%TRR							
Solvent extracts (rinsate+ACN)	**80.38**	**82.57**	**76.28**	**85.83**	**74.09**	**68.11**	**49.11**	**42.56**
Pyrifluquinazon	*55.93*	*48.93*	*54.92*	*70.65*	*31.00*	*28.49*	*17.75*	*12.95*
1H (IV-01)	*13.27*	*18.1*	*1.49*	*2.12*	*23.59*	*21.4*	*5.67*	*7.59*
1H-imino (IV-02)	*0.85*	*1.22*	*0.69*	*0.32*	*2.84*	*2.85*	*1.57*	*4.23*
1H-oxide (IV-03)	*1.08*	*2.17*	*2.48*	*1.01*	*ND*	*ND*	*ND*	*ND*
1H-imino-oxide (IV-04)	*0.06*	*ND*	*0.20*	*0.09*	*ND*	*ND*	*ND*	*ND*
1H-4-oxo (IV-15)	*0.5*	*1.09*	*0.52*	*0.59*	*1.26*	*1.97*	*1.98*	*1.52*
1H-N-Ac (IV-17)	*0.18*	*0.52*	*0.04*	*0.05*	*0.24*	*ND*	*ND*	*ND*
N-Ac (IV-101)	*0.28*	*ND*	*0.37*	*0.32*	*ND*	*ND*	*ND*	*ND*
imino (IV-102)	*0.16*	*0.89*	*0.22*	*0.17*	*ND*	*ND*	*0.14*	*ND*
quinazolinedione (IV-203)	*0.36*	*0.27*	*1.05*	*1.16*	*0.37*	*0.63*	*1.43*	*3.89*
quinazolinone (IV-206)	*0.62*	*0.46*	*1.17*	*0.57*	*0.53*	*0.61*	*0.72*	*0.66*
Total identified	*73.3*	*73.7*	*63.2*	*77.1*	*59.8*	*56.0*	*29.3*	*30.8*
Others	*5.70 (n=17; max 0.9)*	*7.30 (n=12; max 1.0)*	*11.92 (n=15;max 3.2)*	*6.82 (n=25; max 1.3)*	*6.90 (n=5; max 4.8)*	*7.14 (n=3; max 6.6)*	*14.83 (n=7; max 5.1)*	*9.66 (n=2: max 6.3)*
Origin	*1.40*	*1.63*	*1.21*	*1.96*	*7.36*	*5.02*	*5.02*	*2.05*
PES	**19.62**	**17.43**	**23.72**	**14.17**	**25.91**	**31.89**	**50.89**	**57.44**

Component	Leaves				Roots			
	0 DALA	1 DALA	7 DALA	14 DALA	0 DALA	1 DALA	7 DALA	14 DALA
ACN/HCl	*2.33*	*2.64*	*4.19*	*2.3*	*5.77*	*6.28*	*13.19*	*12.46*
ACN/NaOH	*1.76*	*1.62*	*2.39*	*1.17*	*4.34*	*5.30*	*7.81*	*7.62*
Lignin fraction	*3.30*	*2.88*	*5.44*	*3.27*	*4.21*	*6.30*	*9.47*	*10.81*

Parent pyrifluquinazon was the major component in all samples; Pyr-label 9.2–31.3% TRR in roots and 55.7–63.9% TRR in leaves, Qn-label 13.0–31% TRR in roots and 48.9–70.7% TRR in leaves. The major metabolite was 1H (IV-01), which was detected in all samples; Pyr-label 4.1–17% TRR in roots and 2.0–13.8% TRR in leaves, Qn-label 5.7–23.6% TRR in roots and 1.5–18.1% TRR in leaves.

Further metabolites detected at low levels (< 10% TRR) were lH-imino (IV-02), lH-oxide (IV-03), lH-imino-oxide (IV-04), lH-4-oxo (IV-15), quinazolinedione (IV-203), quinazolinone (IV-206) and imino (IV-102). Several minor unidentified metabolites were observed in each sample however, no unidentified metabolite exceeded 10% TRR and 0.01 mg eq/kg.

A proportion of the radioactivity for both labels was associated with lignin fractions (6.3-11.9% TRR).

In summary, the metabolism of pyrifluquinazon in/on radish proceeds predominately through deacetylation of the quinazolinone nitrogen forming 1H (IV-01) and dehydrogenation to imino (IV-102), which may be hydrolysed to the deacetylated metabolite, IH-imino (IV-02). Trace amounts of IH-N-Ac (IV- 17) and N-Ac (IV-101) were detected resulting from intra and inter molecular trans-acetylation of pyrifluquinazon.

Plant metabolism studies have been conducted with Pyr- and Qn-label pyrifluquinazon applied to tomato, lettuce (leafy) and radish plants at rates that accommodate the anticipated maximum total seasonal application rates. The metabolism of pyrifluquinazon is comparable in all three crops investigated. The metabolite 1H (IV-01) is common to all crop metabolism studies and was found in radish leaves, radish roots, lettuce heads and outer leaves and tomato fruit at levels >10% TRR. All other identified metabolites were present in the crop matrices at levels < 10% TRR.

The metabolism of pyrifluquinazon in plants proceeds predominately through deacetylation of the quinazolinone nitrogen forming 1H (IV-01) and dehydrogenation to imino (IV-102), which may be hydrolysed to the deacetylated metabolite, 1H-imino (IV-02). Trace amounts of 1H-N-Ac (IV- 17) and N-Ac (IV-101) were detected resulting from intra and inter molecular trans-acetylation of pyrifluquinazon. Further transformations of 1H (IV-01) occur *via* hydroxylation at the 4-position of the quinazoline ring and oxidation at the 1-position of the pyridine ring and N-N bond cleavage. Metabolites of pyrifluquinazon in plants are shown in Figure 1.

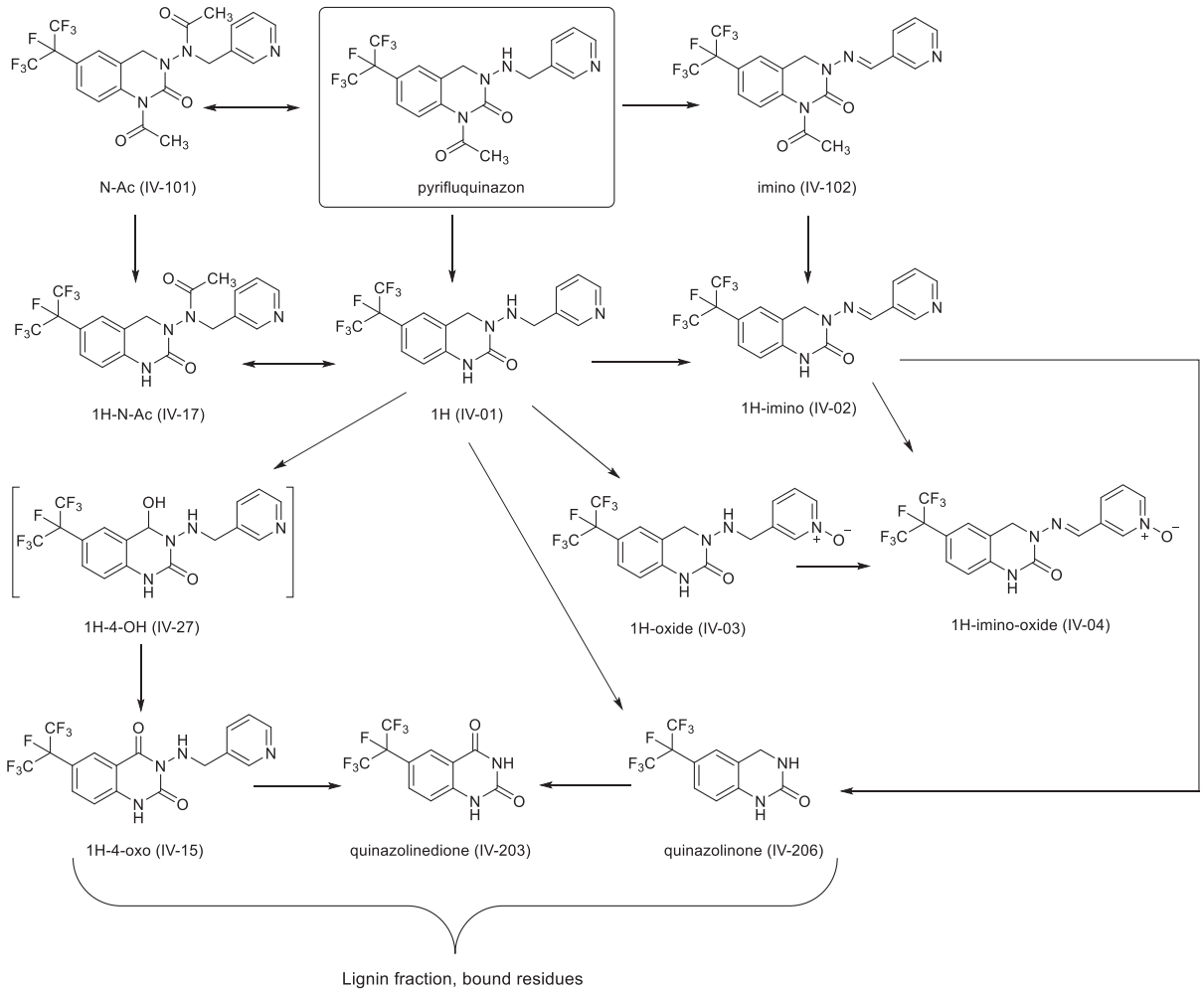


Figure 1 Metabolites of pyrifluquinazon identified in plants

ENVIRONMENTAL FATE

The FAO Manual on the Submission and Evaluation of Pesticide Residues Data for the Estimation of Maximum Residue Levels in Food and Feed (2016) explains the data requirements for studies of environmental fate. The focus should be on those aspects that are most relevant to MRL setting. For pyrifluquinazon, supervised residue trials data are available for radish, lettuce and tomato crops. Aerobic degradation in soil is relevant, as well as the normal requirements for hydrolysis, photolysis and rotational crop studies.

The Meeting received information on soil aerobic metabolism and aqueous and soil hydrolysis properties of pyrifluquinazon. Studies were also received on the behaviour of [^{14}C]-pyrifluquinazon in a confined rotational crop situation.

Pyrifluquinazon residues are not persistent in soils and it is unlikely that pyrifluquinazon residues per se in soils resulting from recommended uses make a significant contribution to the residues in most succeeding crops. Degradation product IV-203 is persistent in soil and may be taken up by plants and detected in follow crops.

Route of degradation in soil

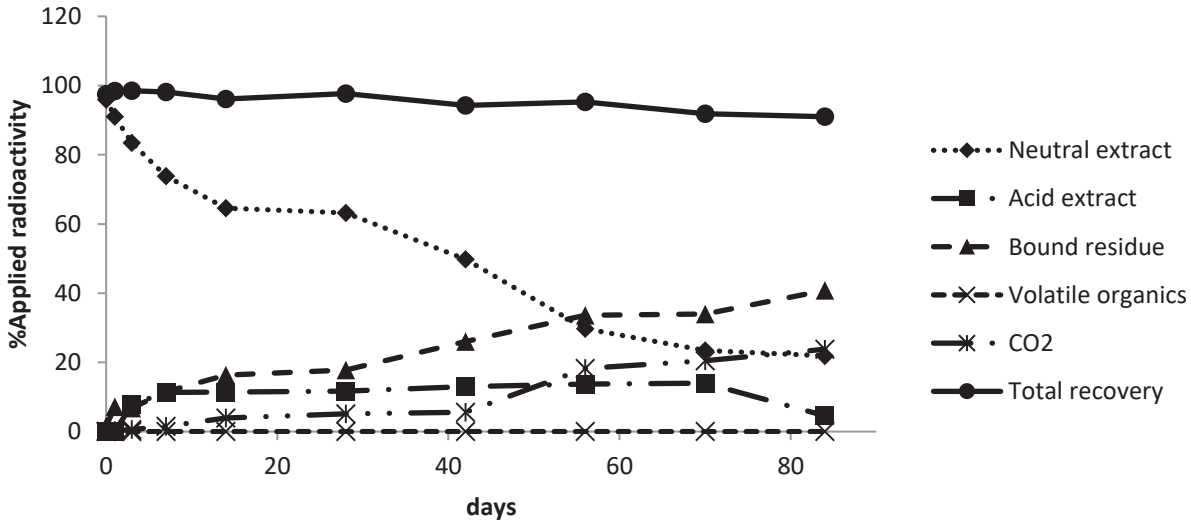
A number of studies were made available on the aerobic soil metabolism of pyrifluquinazon and metabolites.

Aerobic degradation of pyrifluquinazon in soil

Ponte (2010 E-29012) investigated the aerobic soil metabolism of Pyr- and Qn-label pyrifluquinazon on a North Dakota sandy loam soil (sand 26.8%, silt 34.7%, clay 38.5%, organic C 1.12%, pH 7.1, CEC meq/100g 8.6) maintained at 22 °C, 40% MWHC in the dark for up to 84 days. Pyrifluquinazon was incorporated at a nominal concentration of 0.4 mg/kg equivalent to a field application of 300 g ai/ha assuming the test material is evenly applied an incorporated to a depth of 7.5 cm in a soil with bulk density 1 g/cm^3. The soil samples were continuously aerated throughout the incubation period. Traps for volatiles included an ethylene glycol trap to collect organic volatiles and two 10% aqueous NaOH traps to collect CO_2.Samples were extracted with solvent (acetonitrile/ 50 mM sodium ascorbate phosphate buffer adjusted to pH 7 4:1 v:v). The distribution of radioactivity for the two labels is shown in Figure 2.

In the Pyr-label experiment, pyrifluquinazon degraded rapidly, declining from 95% AR at day 0 to 2.5% AR by day 3 (Table 17). The major known metabolites observed were IV-01, IV-02, IV-15, IV-27 and IV-28. A number of unknowns, each individually < 10% TRR were detected. A partition of the humic and fulvic acids from the humin fraction was done to further characterise the soil bound residues for selected samples of soil which contained greater than 10% AR in the soil following extraction. Humic acid and the humin fractions contained an average of 13.0% AR. The fulvic acid fraction contained an average of 14.8% AR.

a) Pyr-label



b) Qn-label

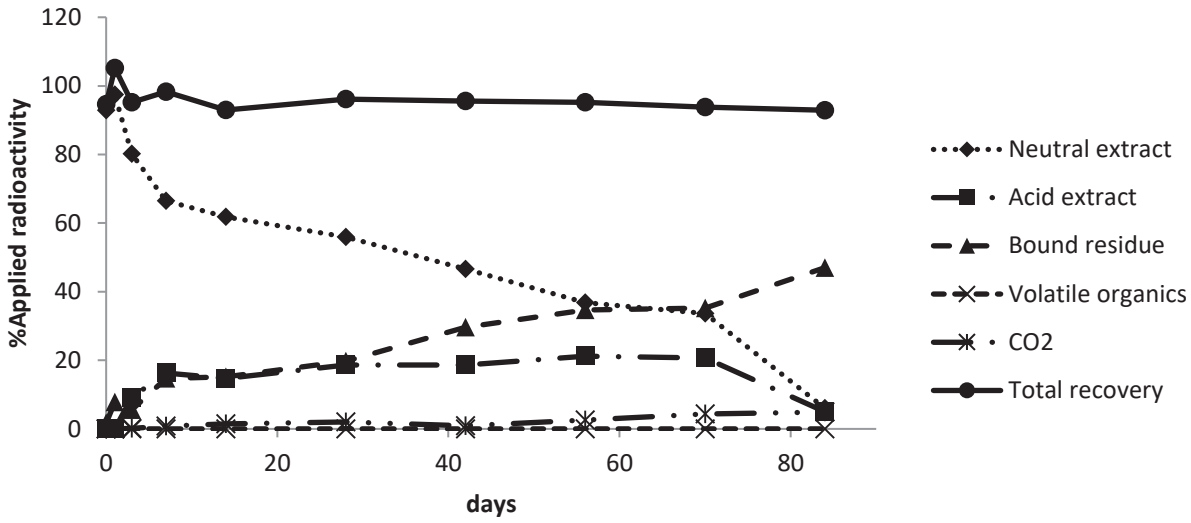


Figure 2a and b Characterisation of aerobic degradation of pyrifluquinazon on a North Dakota sandy loam soil

Pyrifluquinazon Qn-label degraded rapidly in soil under aerobic conditions and represented an average of 92.7% applied radioactivity (AR) at day 0, declining to an average of 7.1% at day 3 and subsequently declining to below detection limits. The major metabolites present in the Qn-label experiment were IV-01, IV-02, IV-15, IV-27, IV-28 and IV-203 (Table 18). A number of unknowns, each individually < 10% TRR were detected.

A partition of the humic and fulvic acids from the humin fraction was done to further characterise the soil bound residues for selected samples of soil which contained greater than 10% AR in the soil following extraction. The smallest component was the fulvic acid fraction, which contained an average of 8.3% AR. The humic acid fraction contained an average of 17.6% AR, and the insoluble humin contained an average of 21.2% AR.

Table 17 Aerobic soil degradates formed in the Pyr-label experiment (%AR).

DAA	0	1	3	7	14	28	42	56	70	84
Pyrifluquinazon	95	17.8	2.5	1.1	0.4	0	0.6	0.1	0	0
IV-01	0.1	53.4	40.8	11.5	2.9	2.3	1.8	1.1	0.8	0.5
IV-02	0	11.7	8.6	11.3	5.4	8.5	2.1	1.8	0.9	0.9
IV-15	0	0.5	7.7	8.2	7.3	6.2	6.9	6	5.5	4.4
IV-27	0	1.7	3.9	13.3	8.3	2	0	2.1	1.2	0.3
IV-28	0	1.5	3.9	8	18.5	14.2	2.9	9.1	3.5	3.3
IV-203	0	0	0	0	0	0	0	0	0	0
DP-1	0	0.2	8.5	14.9	16.1	26.6	36.1	12	16.2	5.2
DP-2	0	1.2	6.2	0.7	0	0	0	0.4	0	0
DP-3	0	0	0	7	7.5	2.4	1.4	1.7	1	0.8
DP-4	0	0	0	0	0	0	1.1	2.2	2.6	3.3
Others	1	3.3	9.2	9.6	9.6	12.9	9.9	7.2	5.9	3.5
Bound	1.6	7.2	6.8	11.5	16.3	17.8	26	33.6	34	40.8

Table 18 Aerobic soil degradates formed in the Qn-label experiment (%AR).

DAA	0	1	3	7	14	28	42	56	70	84
Pyrifluquinazon	92.7	7.8	7.1	2.2	0.6	0	0.9	0.4	0	0
IV-01	0	72.2	45	12.8	3.1	2.8	2.1	2	4.9	0.2
IV-02	0	6.5	15.8	18.7	7.7	3.7	1.4	5.1	4.7	2.1
IV-15	0	0.3	0.9	13.4	10.5	9.6	9	12.5	10.8	7.6
IV-27	0	8.4	1.8	6.9	7.2	2.3	0	4.3	3.4	0.4
IV-28	0	0.5	1.9	8.6	19.8	15.5	6.4	7	4.6	4.8
IV-203	0	0	0	3.6	6.3	10.3	9.7	8.6	8	7.9
IV-303	0	0	0	0	0.8	1.8	0.6	0.3	0	0
DQ-1	0	0	8.6	1	0.6	0	0	0.8	0	0
DQ-2	0	0	0	3.5	7.9	6.8	3.2	2.7	2.1	1.2
DQ-3	0	0	0	0	0	0	5.2	3.5	2.5	5.9
Others	0.2	1.8	9.7	12.1	12.2	22	26.8	11.2	13.6	6.1
Bound	1.7	7.8	5.6	14.7	15.2	19.7	29.6	34.7	35.2	47
Organic	NA	0	0	0	0	0	0	0	0	0
CO_2	NA	0	0.2	0.8	1.5	2	0.9	2.6	4.4	4.9

With the exception of IV-15 and IV-203, pyrifluquinazon and its degradates are not considered persistent in soil. The DT_{50} values for pyrifluquinazon were determined as 0.3 days and 0.1 days for the Pyr- and Qn-label experiments, respectively, with DT_{90} values 1.5 and 0.9 days for the two labels. The DT_{50} and DT_{90} for IV-01, IV-02, IV-15, IV-27, IV-28 and IV-203 were reported (calculated using the non-linear spatial variation model) and are listed in Table 19.

Degradates observed for pyrifluquinazon in soil are displayed in Figure 3.

Table 19 Aerobic soil degradation kinetics for pyrifluquinazon and metabolites

Sample set	α	β	DT_{50} (days)	DT_{90} (days)	r^2
Pyrifluquinazon (Pyr-label)	2.957	0.763	0.3	1.5	0.9999
Pyrifluquinazon (Qn-label)	0.641	39.07	0.10	0.9	0.9993
IV-01 (Qn-label)	5420	4.868E-05	2.6	8.7	0.9903
IV-01 (Pyr-label)	5954	3.63E-05	3.2	10.7	0.9841
IV-02 (Py-label)	2115	1.53E-05	21.4	71.2	0.7907
IV-28 (Qn-label)	2.836	0.0138	20.1	90.7	0.9304
IV-28 (Pyr-label)	2.383	2.04E-02	16.5	79.8	0.7977
IV-15 (Pyr-label)	731	8.75E-06	108	361	0.699
IV-27 (Pyr-label)	7.422	1.20E-02	8	30	0.9592
IV-203 (Qn-label)	0.4398	0.0322	119	5802	0.9658

Qn IV-02, IV-15 and IV-27 were not used in calculation of DT_{50} and DT_{90} due to poor correlation.

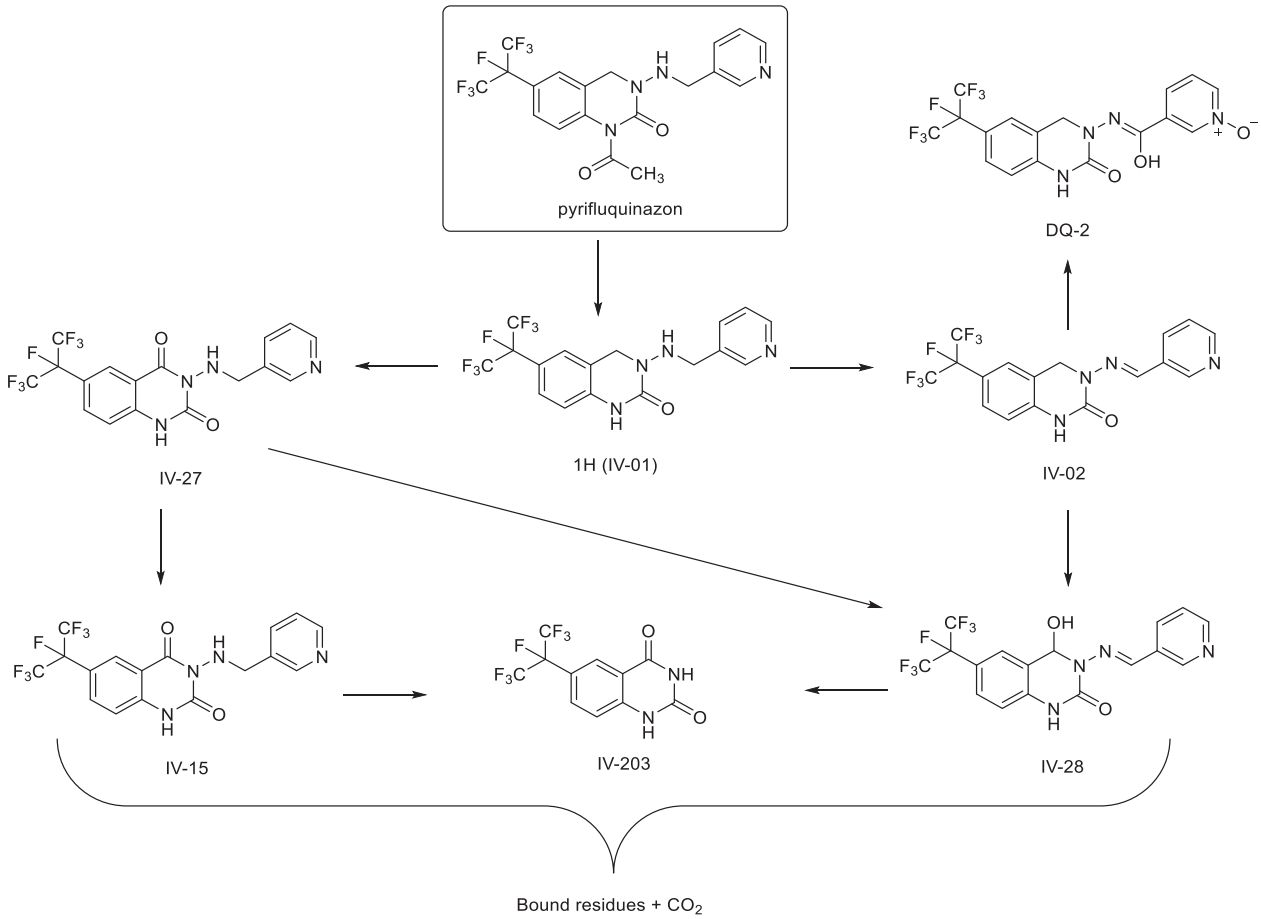


Figure 3 Compounds identified in aerobic soil metabolism

Rate of Degradation in Soil

An aerobic soil degradation rate study for pyrifluquinazon was conducted on three US field soils (Ponte 2010 E-29016). The decline of pyrifluquinazon and the rise and decline of the metabolites found in the aerobic soil route study.

The three soils used for this study were California (designated as CA, sandy loam, sand 69%, silt 20%, clay 11%, organic matter 0.4%, pH 7.6, CEC meq/100g 9.3), Mutchler (designated as MSL soil; sandy loam, sand 62%, silt 19%, clay 19%, organic C 2.0%, pH 6.7, CEC meq/100g 15.5), and Ostlie East (designated OE, clay loam, (sand 43%, silt 28%, clay 29%, organic C 3.2%, pH 7.8, CEC meq/100g 26.9). Individual samples were incubated in the dark at 25 ± 2 °C for at least 2 days prior to treatment and throughout the experiment (for up to 84 days) once they were treated. All samples were maintained aerated in a humidified environment during the study period. Water was added to the soil samples so as to maintain a pF of between 2.0 and 2.5 (approximately 40–60% maximum water holding capacity – MWHC). The dose rate was approximately 0.39 mg/kg pyrifluquinazon. Pyrifluquinazon and its degradates (IV-01, IV-02, IV-27, IV-15, IV-28 and IV-203) were determined by LC-MS.

Pyrifluquinazon degraded very rapidly in CA soil tested and represented < 30% of the applied dose after one day of incubation, and subsequently falling below LOQ (Table 20). Pyrifluquinazon degraded at slower rates in MSL (Table 21) and OE (Table 22) soils and represented 75.1% and 51.7% after 1 day of incubation, respectively. IV-01, IV-02, IV-27 and IV-28 were present in all soils, while IV-15 was present only in MSL soils and IV-203 was present only at one time point in OE soil samples.

Table 20 Aerobic soil degradates formed in the California sandy loam (%AD).

DAA	0	1	3	7	14	28	56
Pyrifluquinazon	89	29.5	0	0	0	0	0
IV-01	0	33.2	56.7	18.2	1.7	0	0
IV-02	0	8.4	8.5	14.7	5.7	4.5	3.2
IV-15	0	0	0	0	2.4	0	0
IV-27	0	10.8	16.8	14.3	2.6	0	0
IV-28	0	0	0	13.6	16	3.2	0
IV-203	0	0	0	0	0	4.9	3.5

Table 21 Aerobic soil degradates formed in the Mutchler sandy loam (%AD).

DAA	0	1	3	7	14	27	55	83
Pyrifluquinazon	104.1	75.1	32	9	5.3	22.5	7.9	4
IV-01	0	18.2	24.2	9.5	2.9	6.5	1.9	0
IV-02	1.4	6.4	9.9	10.5	14.1	14.9	12	8.7
IV-15	0	0	0	1.9	1.6	1.1	0.9	1
IV-27	0	4.1	20.6	16.2	1.3	4.4	2.4	0
IV-28	0	0	5.2	5.3	16.8	3.8	4.9	1.5
IV-203	0	0	0	0	0	0	1.1	0

Table 22 Aerobic soil degradates formed in the Ostlie East clay loam (%AD).

DAA	0	1	3	7	13	27	55	83
Pyrifluquinazon	112.8	51.7	33.3	14.3	18.4	17.6	1.8	0
IV-01	0	55.3	45.1	32.9	16.7	35.1	15.4	10
IV-02	0	1.2	3.2	4.8	2.8	7.8	13	9.9
IV-15	0	0	0	0	0	0	1	1.4
IV-27	0	2	3.9	6.8	2.5	7	8.3	6
IV-28	0	0	0	3.3	1.7	2	6.1	14.2
IV-203	0	0	0	4.4	1.2	0	1.4	1.7

DT_{50} values of pyrifluquinazon for all experiments were determined based on the percent pyrifluquinazon present in the soil extracts, using either first-order kinetics (CA soil) or the multi-compartment Gustafson-Holden model (MSL and OE soils). The half-lives for the metabolites were calculated using first order kinetics, with the time point where the maximum average was observed as the initial point in the degradation curve (Table 23).

Table 23 Aerobic soil degradation kinetics for pyrifluquinazon and metabolites in three US soils

	DT_{50} (days)	DT_{90} (days)	r^2
CA soil pyrifluquinazon	0.6	2.1	1.000
MSL soil pyrifluquinazon	1.7	12.0	0.9421
OE soil pyrifluquinazon	0.8	37.9	0.9647
CA soil, IV-01	2.2	7.2	0.998
MSL soil, IV-01	16.5	54.7	0.910
OE soil, IV-01	43.3	144	0.622
CA soil, IV-02	27.7	92	0.710

	DT_{50} (days)	DT_{90} (days)	r^2
MSL soil, IV-02	77	256	0.987
MSL soil, IV-027	16.9	56.1	0.934
MSL soil, IV-028	25.7	85	0.735

Aerobic soil metabolism is a significant route of degradation for pyrifluquinazon in the environment. Some degradates are moderately (IV-01) to somewhat persistent (IV-02, IV-15, IV-203) in the environment.

Environmental fate in water

Hydrolysis

Lopez (2009 E-29010) studied the hydrolytic stability of [^{14}C]-pyrifluquinazon (1.0 mg/L; Qn-label) at 25 °C for up to 31 days in dark, sterile, aqueous buffered solutions at pH 5, 7 and 9. Average radiocarbon recoveries ranged between 98.2 ± 4.0% and 101.8 ± 3.3% of the applied radiocarbon.

Pyrifluquinazon degraded slowly in pH 5 buffer systems and represented an average of 84.3% AR after 31 days of incubation. The major degradate observed was IV-01, and represented an average of 13.1% AR at the end of the study. Pyrifluquinazon degraded much faster in neutral and basic pH buffers and represented an average of 41.6% AR in pH 7 samples after 31 days of incubation. In pH 9 samples, pyrifluquinazon represented an average of 40.6% AR after only 1 day of incubation. IV-01 was also the major degradate observed in pH 7 and pH 9 samples and represented an average of 56.8% AR in pH 7 samples (31 days of incubation) and 47.7% AR in pH 9 samples (after 1 day of incubation).

The DT_{50} of hydrolysis of pyrifluquinazon in aqueous buffer samples was calculated based on the percent test substance present in the aqueous solutions, assuming pseudo-first order kinetics (Table 24).

Table 24 Rates of aqueous hydrolysis for pyrifluquinazon

Sample set	Rate constant ($days^{-1}$)	DT_{50} (days)	r^2
pH 5	–0.00730	94.9	0.6968
pH 7	–0.0292	23.7	0.9838
pH 9	–0.0335	0.9 (20.7 hours)	0.9930

Aqueous hydrolysis is expected to contribute significantly to the degradation of pyrifluquinazon in the environment.

Photochemical degradation

Soil photolysis

Lopez (2010 E-29015) studied the soil photolysis of [^{14}C]-pyrifluquinazon (Pyr- and Qn-labels) on sterile sandy loam (sand 77%, silt 14%, clay 9%, organic C 2.7%, pH 7.5, CEC mval/100 g 14.6) at 25 °C. Samples were irradiated using a Xe lamp (465 W/m^2 300-800 nm). The radioactivity extracted using acetonitrile/50 mM Na ascorbate pH 7 (4/1 v/v) decreased with time as the ‘bound’ or unextracted radioactivity increased. Pyrifluquinazon is rapidly degraded in soil under aerobic conditions with little difference between dark control and irradiated samples. The main compounds detected were IV-01, IV-02, IV-15, IV-27, IV-28 and IV-102. The soil photolysis half-life is determined as “stable” as the half-life in the irradiated samples was longer than the half-life in the dark controls.

Photochemical degradation is not expected to contribute significantly to the degradation of pyrifluquinazon in the environment.

Confined rotational crop studies

A confined rotational crop study was conducted on an outdoor plot of sandy loam soil (Grangeville fine sandy loam: 70% sand, 18% silt, 12% clay; pH 7.5; 0.6% organic matter; 9.2 meq/100 g CEC) which had been treated with Pyr- or Qn-label at 206 g ai/ha (*ca*. 2-2.6N maximum seasonal rate) (Quistad and LaMar, 2010 R-29047). Rotational crops (lettuce cv Salad bowl, radish cv Crimson Giant and wheat cv Summit) sown into the soil at 30, 120 and 360 (419 for lettuce) days after the application (DAA) for the Pyr-label experiment and at 30, 120 and 390 (434 for lettuce) DAA for the Qn-label experiment. Plants were collected at various intervals for measurement of radioactivity by combustion analysis. The samples were extracted within two months of harvest and analysed within two months of initial extraction.

All samples were frozen and homogenized in presence of dry ice. Samples were extracted twice with acetonitrile and then the solids separated by centrifugation or vacuum filtration. Further extractions were conducted with acetonitrile/water (1:1, v/v). PES containing residues > 0.01 mg eq/kg or > 10 %TRR were hydrolysed with 0.1M and 24% KOH in water. In certain cases, these basic extracts were acidified and partitioned between ethyl acetate and water. HPLC analysis was performed on combined extracts. Co-injection of reference standards allowed for metabolite identification and confirmation of identity was achieved with 2D TLC.

Samples from the Pyr-label experiment had lower TRR than for the Qn-label experiment (Table 25). Additionally, the TRR for all RACs was lower at the 120-day PBI (autumn) with higher but similar levels observed for the 30-day and ≥ 360-day PBIs (summer).

Table 25 Distribution of radioactivity in rotational crops after treatment of soil with [^{14}C]-pyrifluquinazon (Quistad and LaMar, 2010 R-29047)

DAA	Average total residue (mg equiv/kg)							
	Immature lettuce	Mature lettuce	Radish foliage	Radish root	Wheat forage	Wheat hay	Wheat straw	Wheat grain
Pyr-label								
30	0.003	0.002	0.004	0.004	0.015	0.023	0.019	0.010
120	0.002	< 0.001	0.002	0.001	0.003	0.009	0.007	0.003
360			0.002	0.002	0.004	0.017	0.038	0.007
419	0.001	0.002						
Qn-label								
30	0.015	0.018	0.080	0.014	0.107	0.218	0.160	0.006
120	0.011	0.005	0.032	0.008	0.027	0.031	0.089	0.004
390	0.030		0.055	0.008	0.062	0.136	0.296	0.006
434		0.011						

Extraction efficiencies for Qn-label experiment were generally good with the solvent system used (acetonitrile/H_2O) and were > 60% for lettuce, > 84% for radish foliage and roots, > 88% for wheat forage, > 50% for wheat hay, > 60% for straw and > 65% for grain (Table 26).

Table 26 Extraction efficiency in plant matrices

Matrix	**Extraction conditions**	**%TRR (mg/kg)**					
		Pyr-label			**Qn-label**		
		30 DAA	**120 DAA**	**360 DAA[a]**	**30 DAA**	**120 DAA**	**390 DAA[b]**
Immature Lettuce	**Solvent extracted** *ACN*	**NA** *NA*	**NA** *NA*	**NA** *NA*	**87.5** *87.5*	**90.9** *81.8*	**71.9** -

Matrix	Extraction conditions	%TRR (mg/kg)					
		Pyr-label			Qn-label		
		30 DAA	120 DAA	360 DAA[a]	30 DAA	120 DAA	390 DAA[b]
	ACN/H_2O	-	-	-		*9.1*	*71.9*
	PES	**-**	**-**	**-**	**12.5**	**9.1**	**28.1**
	0.1M KOH	-	-	-	-	-	*3.1*
	24% KOH	-	-	-	-	-	*25.0*
Mature Lettuce	**Solvent extracted**	**NA**	**NA**	**NA**	**92.9**	**NA**	**61.1**
	ACN	*NA*	*NA*	*NA*	*78.6*	*NA*	-
	ACN/H_2O	-	-	-	*14.3*	-	*61.1*
	PES	**-**	**-**	**-**	**7.1**	**-**	**38.9**
	KOH	-	-	-	*NA*	-	*38.9*
Radish Foliage	**Solvent extracted**	**NA**	**NA**	**NA**	**95.7**	**96.8**	**84.8**
	ACN	*NA*	*NA*	*NA*	*91.5*	*90.3*	-
	ACN/H_2O	-	-	-	*4.2*	*6.5*	*84.8*
	PES	**-**	**-**	**-**	**4.2**	**3.2**	**15.2**
	24% KOH	-	-	-	-	-	*15.2*
Radish Root	**Solvent extracted**	**NA**	**NA**	**NA**	**84.6**	**88.9**	**88.9**
	ACN	*NA*	*NA*	*NA*	*76.9*	*88.9*	-
	ACN/H_2O	-	-	-	*7.7*	-	*88.9*
	PES	**-**	**-**	**-**	**15.4**	**11.1**	**11.1**
Wheat forage	**Solvent extracted**	**60.0**	**NA**	**NA**	**90.8**	**96.3**	**88.7**
	ACN	*33.3*	*NA*	*NA*	*78.6*	*85.2*	-
	ACN/H_2O	*26.7*	-	-	*12.2*	*11.1*	*88.7*
	PES	**40.0**	**-**	**-**	**9.2**	**3.7**	**11.3**
Wheat Hay	**Solvent extracted**	**28.2**	**55.5**	**30.3**	**69.1**	**71.9**	**51.6**
	ACN	*7.7*	*11.1*	-	*42.5*	*25.0*	-
	ACN/H_2O	*20.5*	*44.4*	*30.3*	*26.6*	*46.9*	*51.6*
	PES	**71.8**	**44.5**	**69.7**	**30.9**	**28.1**	**48.4**
	0.1M KOH	-	-	-	-	-	*13.0*
	24% KOH	*61.5*	-	*57.6*	*26.2*	-	*26.7*
Wheat Straw	**Solvent extracted**	**41.7**	**NA**	**15.9**	**75.2**	**65.7**	**68.1**
	ACN	*12.5*	*NA*	-	*51.0*	-	-
	ACN/H_2O	*29.2*	-	*15.9*	*24.2*	*65.7*	*68.1*
	PES	**59.3**	**-**	**84.1**	**24.8**	**34.3**	**31.9**
	0.1M KOH	*45.8*	-	*20.5*	*19.0*	*27.8*	*9.5*
	24% KOH	-	-	*43.2*	-	-	*16.1*
Wheat Grain	**Solvent extracted**	**30.0**	**NA**	**NA**	**66.7**	**NA**	**NA**
	ACN	*0.0*	*NA*	*NA*	*0.0*	*NA*	*NA*
	ACN/H_2O	*30.0*	-	-	*66.7*	-	-
	PES	**70.0**	**-**	**-**	**33.3**	**-**	**-**

[a] For lettuce, 419 DAA

[b] For mature lettuce, 434 DAA

Parent pyrifluquinazon was not detected in any matrix. Solvent extracts of Pyr-label wheat forage, hay, straw, and grain were analysed by HPLC but no metabolites at ≥0.01 mg eq/kg were detected.

In the Qn-label experiment, the predominant residue detected in follow crops was quinazolinedione (IV-203) and its conjugate. 1H-4-oxo (IV-15) was found only in 30 day wheat forage (0.020 mg eq/kg).

The metabolites/degradates identified in the rotational crops are presented in Tables 27 to 30.

For 30/120 DAA to soil with Qn-label, quinazolinedione (IV-203) was found in lettuce (0.001–0.002 mg eq/kg), radish foliage (0.025–0.034 mg eq/kg), radish roots (0.006 mg eq/kg), wheat forage/hay/straw (0.010–0.026 mg eq/kg), wheat grain (0.001 mg eq/kg, 30 day only). At 390 DAA, quinazolinedione (IV-203) was > 0.01 mg equiv /kg for radish foliage (0.017 mg eq/kg), wheat hay (0.015 mg eq/kg), and wheat straw (0.047 mg eq/kg). A labile conjugate of quinazolinedione occurred at > 0.01 mg equiv /kg in radish foliage (0.013 mg eq/kg, 30 day), wheat forage (0.022 mg eq/kg, 390 day), wheat hay (up to 0.066 mg equiv /kg, 30 day), wheat straw (up to 0.048 mg eq/kg, 390 day) but not wheat grain (< 0.001 mg eq/kg).

Table 27 Identification of residues in lettuce as a rotational crop from the Qn-label experiment

LETTUCE	immature			Mature		
DAA	30	120	390	30	120	434
TRR (mg equiv/kg)	0.015	0.011	0.030	0.018	0.005	0.011
	%TRR					
quinazolinedione (IV-203)	6.3	18.2	ND	14.3	NA	11.1
1H-4-oxo (IV-15)	ND	ND	ND	ND	-	ND
Conjugate of quinazolinedione (IV-203)	25.0	63.6	31.3	35.7	-	27.8
Total identified	*31.3*	*81.8*	*31.3*	*50.0*	-	*38.9*
C2 [a]	ND	ND	ND	ND	-	ND
Unknown, C3	31.3	ND	ND	28.6	-	16.7
Sum of others	25.0	9.1	21.9	14.3	-	0.6
Max. other single [b]	12.5	-	18.8	7.1	-	< 0.6

[a] C2 is an HPLC fraction that contains in part the conjugate of quinazolinedione (IV-203)

[b] Maximum other component in acetonitrile/water extracts

Table 28 Identification of residues in radish as a rotational crop from the Qn-label experiment

RADISH	Foliage			Roots		
DAA	30	120	390	30	120	390
TRR (mg equiv/kg)	0.080	0.032	0.055	0.014	0.008	0.008
	%TRR					
quinazolinedione (IV-203)	47.9	80.6	37.0	46.2	66.7	22.2
1H-4-oxo (IV-15)	ND	ND	ND	ND	ND	ND
Conjugate of -quinazolinedione (IV-203)	18.3	12.9	ND	<7.7	<11.1	ND
aminoquinazolinone-N-Ac (IV-208)	-	3.2	-	-	Trace	-
Total identified‡	*66.2*	*93.5*	*37.0*	*53.9*	*77.8*	*22.2*
C2 [a]	9.9	ND	ND	ND	<11.1	ND
Unknown, C3	8.5	ND	ND	7.7	<11.1	ND
Sum of others	11.3	3.2	47.8	15.4	22.2	66.7
Max. other single [b]	8.5	3.2	10.9	7.7	11.1	44.4

[a] C2 is an HPLC fraction that contains in part the conjugate of quinazolinedione (IV-203)

[b] Maximum other single component in acetonitrile/water extracts

Table 29 Identification of residues in wheat as a rotational crop from the Pyr-label experiment

WHEAT	Forage			Hay			Straw			Grain		
DAA	30	120	360	30	120	360	30	120	360	30	120	360
TRR (mg equiv/kg)	0.015	0.003	0.004	0.023	0.009	0.017	0.019	0.007	0.038	0.010	0.003	0.007
	%TRR											
Nicotinic acid related [a]	26.7	NA	NA	20.5	NA	ND	29.2	NA	-	10.0	NA	NA
Sum of others	33.3	-	-	7.7	-	30.3	12.5	-	15.9	20.0	-	-

WHEAT	Forage			Hay			Straw			Grain		
DAA	30	120	360	30	120	360	30	120	360	30	120	360
TRR (mg equiv/kg)	0.015	0.003	0.004	0.023	0.009	0.017	0.019	0.007	0.038	0.010	0.003	0.007
Max. other single [b]	13.3	-	-	5.1	-	12.1	8.3	-	6.8	<10.0	-	-

[a] Residues were in such low concentrations, positive identification could not be accomplished.

[b] Maximum other single component in acetonitrile/water extracts

Table 30 Identification of residues in wheat as a rotational crop from the Qn-label experiment

	Forage			Hay			Straw			Grain		
DAA	30	120	390	30	120	390	30	120	390	30	120	365
TRR (mg equiv/kg)	0.107	0.027	0.062	0.218	0.031	0.136	0.160	0.089	0.296	0.006	0.004	0.006
	%TRR											
quinazolinedione (IV-203)	19.4	48.1	9.4	8.9	31.3	9.3	17.0	19.4	16.5	16.7	NA	NA
1H-4-oxo (IV-15)	20.4	ND	ND	ND	ND	ND	ND	ND	ND	ND	NA	NA
Conjugate of quinazolinedione (IV-203)	9.2	14.8	41.5	30.8	ND	14.9	19.6	ND	16.8	ND	NA	NA
Total identified	*49.0*	*62.9*	*50.9*	*39.7*	*31.3*	*24.2*	*36.6*	*19.4*	*33.3*	*16.7*	*NA*	*NA*
C2 [a]	20.4	22.2	20.8	15.9	18.8	17.4	15.0	21.3	29.1	ND	-	-
Unknown, C3	5.1	ND	7.5	8.9	ND	ND	11.1	ND	ND	ND	-	-
Sum of others	16.3	11.1	9.4	4.7	21.9	9.9	12.4	25.0	5.6	50.0	-	-
Max. other single [b]	3.1	3.7	5.7	1.9	6.3	1.9	5.9	4.6	2.5	16.7	-	-

[a] C2 is an HPLC fraction that contains in part the conjugate of quinazolinedione (IV-203)

[b] Maximum other single component in acetonitrile/water extracts

The compounds identified in rotational crops are shown in Figure 4.

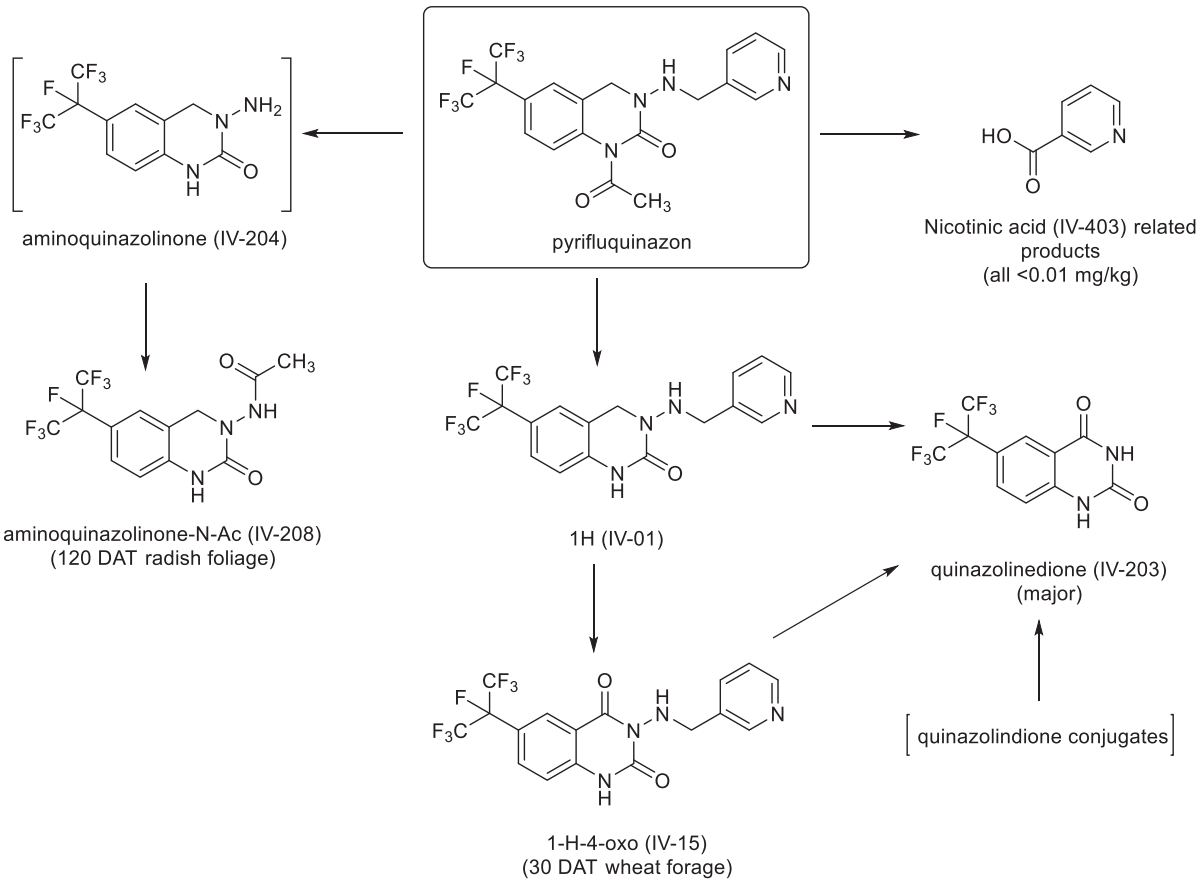


Figure 4 Compounds identified in rotational crops

Field rotational crop trials on representative crops

Carringer (2011 R-29108) studied the magnitude of pyrifluquinazon and metabolite quinazolinedione (IV-203) in succeeding crops following spray application of an SC formulation of pyrifluquinazon to a primary crop of mustard greens. In the two field trials (plot sizes 669 m^2), three foliar applications were made each at a rate of 101 g ai/ha in water volumes of 140–309 L/ha, at 15, 8–9 and 1 day before harvest of the primary crop. A non-ionic surfactant was added to the spray solution at a rate of 0.25–0.5% v/v. The mustard greens primary crop was harvested 1 day after the last application and the rotational crops (radish, leaf lettuce and sorghum) were planted at three PBIs; 13–14, 29–30 and 58–60 days. Radish roots and tops and leaf lettuce were sampled at normal commercial harvest (ca. BBCH 47–49). Sorghum forage was collected at the late dough/early dent stage (BBCH 85-87) and sorghum grain and stover samples were collected at BBCH 89. All samples were frozen the same day as sampling. Samples were stored for a maximum of 124 days prior to analysis. Samples were analysed for pyrifluquinazon and IV-203 using a method with an LOQ of 0.01 mg/kg and LOD of 0.003 mg/kg, for all analytes. Procedural recoveries provided on radish, lettuce and sorghum forage, grain and stover demonstrated acceptable performance of the method.

Pyrifluquinazon residues in all crop matrices at all PBIs were < LOQ (0.01 mg/kg) and in most cases < LOD (0.003 mg/kg) (Table 31). Residues of IV-203 in radish roots were in general < 0.01 mg/kg apart from samples at 30 and 58 day PBIs where a maximum residue of 0.0148 mg/kg was detected. In radish tops residues were observed in the range 0.0117–0.155 mg/kg. IV-203 was not detected in lettuce at any plant back interval. IV-203 was detected in sorghum forage in the range 0.0103–0.0139 mg/kg at 30 and 58 day PBIs. IV-203 was < 0.01 mg/kg in sorghum grain except at 13 day PBI where a single residue of 0.0143 mg/kg was observed. IV-203 in sorghum stover was detected at 14, 30 and 58 day PBIs where residues ranged from < 0.01–0.0194 mg/kg.

Table 31 Pyrifluquinazon residues in rotational crops resulting from field trials in the USA (Carringer 2011 R-29108)

Crop	Commodity	Harvest DAP [a]	PBI (days)	Residues (mg/kg) Pyrifluquinazon	IV-203 [b]	SUM [b]
Uvalde, TX, USA, 2010						
Radish	Roots Tops	51 51	13	< 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003)	< 0.01 < 0.01 (< 0.01) 0.0652 0.0395 (0.0524)	< 0.01 < 0.01 (< 0.01) 0.0652 0.0395 (0.0524)
Leaf lettuce	Leaves	43		< 0.003 < 0.003 (< 0.003)	< 0.003 < 0.003 (< 0.003)	< 0.01 < 0.01 (< 0.01)
Sorghum	Forage Grain Stover	80 109 109		< 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003)	< 0.003 < 0.003 (< 0.003) < 0.01 0.0143 (< 0.0122) < 0.01 < 0.01 (< 0.01)	< 0.01 < 0.01 (< 0.01) < 0.01 0.0143 (< 0.0122) < 0.01 < 0.01 (< 0.01)
Radish	Roots Tops	44 44	29	< 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003)	< 0.01 < 0.01 (< 0.01) 0.0744 0.0730 (0.0737)	< 0.01 < 0.01 (< 0.01) 0.0744 0.0730 (0.0737)
Leaf lettuce	Leaves	44		< 0.003 < 0.003 (< 0.003)	< 0.003 < 0.003 (< 0.003)	< 0.01 < 0.01 (< 0.01)
Sorghum	Forage Grain Stover	83 100 100		< 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003)	< 0.01 < 0.003 (< 0.01) < 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003)	< 0.01 < 0.01 (< 0.01) < 0.01 < 0.01 (< 0.01) < 0.01 < 0.01 (< 0.01)
Radish	Roots Tops	40 40	60	< 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003)	< 0.01 < 0.01 (< 0.01) 0.0117 0.0153 (0.0135)	< 0.01 < 0.01 (< 0.01) 0.0117 0.0153 (0.0135)
Leaf lettuce	Leaves	40		< 0.003 < 0.003 (< 0.003)	< 0.003 < 0.003 (< 0.003)	< 0.01 < 0.01 (< 0.01)
Sorghum	Forage Grain Stover	76 124 124		< 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003)	< 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003)	< 0.01 < 0.01 (< 0.01) < 0.01 < 0.01 (< 0.01) < 0.01 < 0.01 (< 0.01)
Porterville, CA, USA, 2010						
Radish	Roots Tops	41 41	14	< 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003)	< 0.01 < 0.01 (< 0.01) 0.0747 0.0603 (0.0675)	< 0.01 < 0.01 (< 0.01) 0.0747 0.0603 (0.0675)
Leaf lettuce	Leaves	63		< 0.003 < 0.003 (< 0.003)	< 0.01 < 0.01 (< 0.01)	< 0.01 < 0.01 (< 0.01)
Sorghum	Forage Grain Stover	98 134 134		< 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003)	< 0.01 < 0.01 (< 0.01) < 0.003 < 0.003 (< 0.003) < 0.01 0.0126 (< 0.0113)	< 0.01 < 0.01 (< 0.01) < 0.01 < 0.01 (< 0.01) < 0.01 0.0126 (< 0.0113)

Crop	Commodity	Harvest DAP [a]	PBI (days)	Residues (mg/kg) Pyrifluquinazon	IV-203 [b]	SUM [b]
Radish	Roots Tops	47 47	30	< 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003)	< 0.01 0.0111 (0.0103) 0.0842 0.104 (0.0941)	< 0.01 0.0111 (0.0103) 0.0842 0.104 (0.0941)
Leaf lettuce	Leaves	82		< 0.003 < 0.003 (< 0.003)	< 0.003 < 0.003 (< 0.003)	< 0.01 < 0.01 (< 0.01)
Sorghum	Forage Grain Stover	101 131 131		< 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003)	0.0103 0.0110 (0.0107) < 0.003 < 0.003 (< 0.003) 0.0102 < 0.01 (< 0.0101)	0.0103 0.0110 (0.0107) < 0.01 < 0.01 (< 0.01) 0.0102 < 0.01 (< 0.0101)
Radish	Roots Tops	40 40	58	< 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003)	0.0122 0.0148 (0.0135) 0.151 0.155 (0.153)	0.0122 0.0148 (0.0135) 0.151 0.155 (0.153)
Leaf lettuce	Leaves	73		< 0.003 < 0.003 (< 0.003)	< 0.003 < 0.003 (< 0.003)	< 0.01 < 0.01 (< 0.01)
Sorghum	Forage Grain Stover	88 126 126		< 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003) < 0.003 < 0.003 (< 0.003)	0.0137 0.0139 (0.0138) < 0.003 < 0.003 (< 0.003) 0.0194 0.0177 (0.0186)	0.0137 0.0139 (0.0138) < 0.01 < 0.01 (< 0.01) 0.0194 0.0177 (0.0186)

[a] Days between sowing and sampling the succeeding crop

[b] Residues expressed as pyrifluquinazon equivalents. Means for IV-203 calculated assuming levels <LOQ are present at the LOQ. Pyrifluquinazon levels <LOD are assumed to be 0.

Uvalde: radish cv Crunchy Red, leaf lettuce cv Black-seeded Simpson, sorghum cv A571

Porterville: radish cv Crimson Giant, leaf lettuce cv Tango, sorghum cv 84G62

Residues of IV-203 may be expected in follow crops.

ANIMAL METABOLISM

Laboratory animal studies

Metabolism of pyrifluquinazon in rats was evaluated by the WHO Core Assessment Group of the 2019 JMPR. Metabolites identified in rats included IV-01, IV-02, IV-03, IV-04, IV-15, IV-27, IV-203, IV206, IV-208, IV-211, IV-303, IV-403, IV-404 and IV-405.

Lactating goat

The metabolism and distribution of ^{14}C-pyrifluquinazon was investigated in two lactating goats (47 kg bw) following repeated oral administration by gelatine capsule (Quinstad and LaMar 2009, amended 2013 R-29058). Pyrifluquinazon was administered daily on five consecutive days at a dose level of 0.6–0.7 mg/kg bw (corresponding to approximately 12 ppm in the diet for the Pyr-label and 11 ppm for the Qn-label based on daily feed consumption during the acclimatisation period of 2.7 (Pyr expt) and 2.8 (Qn-expt) kg/day respectively). Mean milk production during the dosing period was 0.43 and 1.84 kg/day respectively. Animals were euthanized approximately 20–22 hours after that last dose. Liver, kidney, muscle and fat were extracted and analysed by HPLC and TLC within 108 days of sacrifice. Selected milk samples (day 4 PM) were extracted and analysed within 90 days of sacrifice.

Following the administration of ^{14}C pyrifluquinazon, radioactivity is excreted via faeces (44–55%) and urine (12–14%) by 20–22 hours after the last dose. Milk accounted for 0.4–3% administered dose (AD) while tissues accounted for 7–20% AD (Table 32). The material balance was 90% AD.

TRR were highest for liver (5.355–14.268 mg eq/kg), followed by kidney (0.810–2.450 mg eq/kg). Muscle and fat had low residues (0.137–0.567 and 0.149–0.312 mg eq/kg, respectively).

Table 32 Distribution of ^{14}C following administration of [^{14}C]-pyrifluquinazon for five days (Quinstad and LaMar 2009, amended 2013 R-29058).

	Pyr-label		Qn-label	
	%AD	mg equiv/kg	%AD	mg equiv/kg
Tissues	**20.1** [a]		**6.96** [a]	
Liver		*14.268*		*5.355*
Kidney		*2.450*		*0.810*
Fat (omental)		*0.149*		*0.225*
Fat (subcutaneous)		*0.312*		*0.203*
Fat (renal)		*0.193*		*0.232*
Muscle (flank)		*0.482*		*0.143*
Muscle (loin)		*0.567*		*0.137*
Bile	**0.07**	**6.663**	**0.05**	**4.997**
Blood	**0**	**0.169**	**0**	**0.214**
Milk (total)	**0.39**		**3.07**	
Excreta	**56.1**		**68.9**	
Faeces	*44.5*		*55.06*	
Urine	*11.6*		*13.86*	
GI tract	**13.05**		**10.99**	
Cage wash	**0.04**		**0.09**	
Total	**89.7**		**89.7**	

[a] Calculated assuming fat and muscle are 12 and 40% respectively of body weight

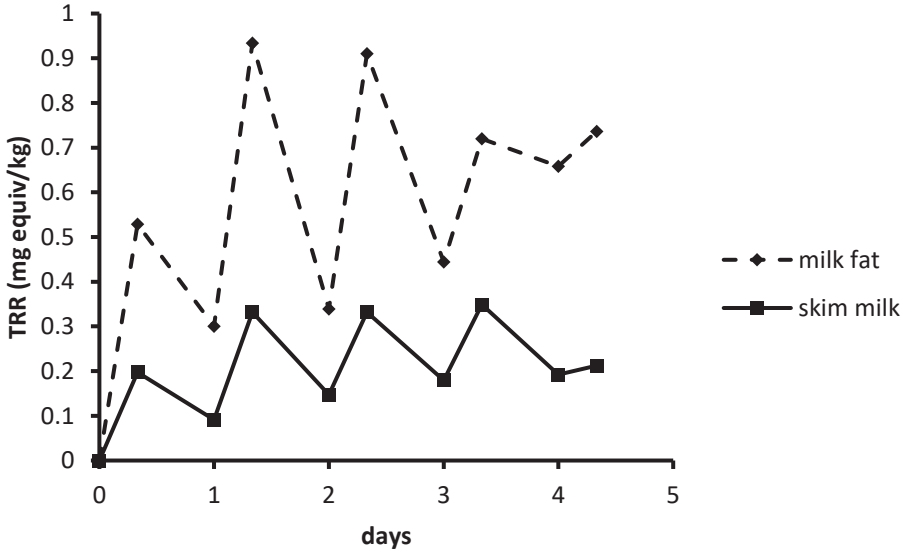


Figure 5a Residues in milk following dosing with ^{14}C-pyrifluquinazon, Pyr-label

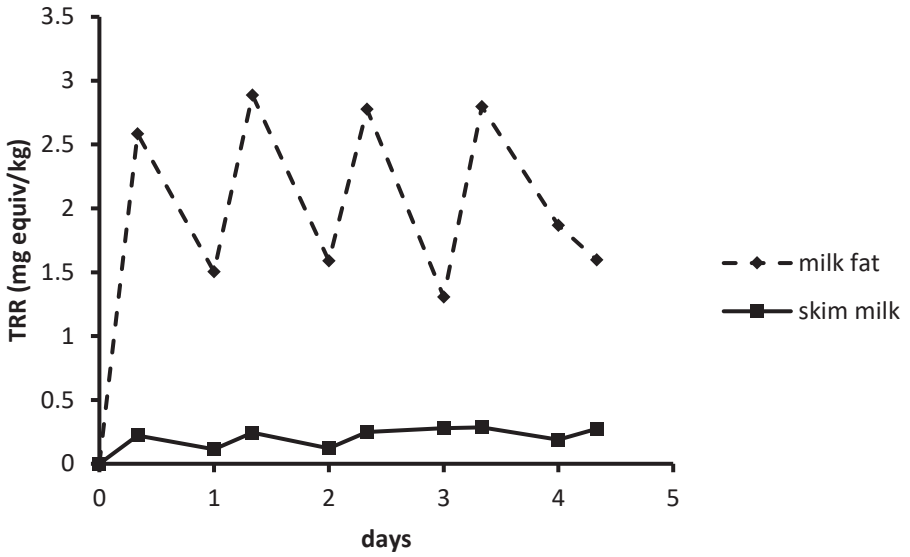


Figure 5b Residues in milk following dosing with ^{14}C-pyrifluquinazon, Qn-label.

Residues in milk appeared to reach a plateau by day four of dosing (Figures 5a and b). There were significant differences in ^{14}C levels between milk collected one hour after dosing compared to eight hours, suggesting pyrifluquinazon residues are rapidly eliminated following dosing.

A range of extraction schemes were used to further characterise residues in milk and tissues.

Skim milk was separated from milk fat by centrifugation prior to analysis of ^{14}C radioactivity. Milk fat was analysed separately from skim milk. Milk samples with the highest residue present (typically Day 4 pm) were selected for extraction.

Skim milk. Protein was precipitated from skim milk by adding acetone and chilling. The protein pellet was then extracted with twice with acetone/H_2O (1:1, v/v). Skim milk and protein pellet acetone extracts were combined, concentrated and analysed directly by both HPLC and 2D TLC.

Milk fat was extracted twice with acetone/hexane (1:1, v/v) and then acetone. The organic extracts were separated from solids by centrifugation. The aqueous layer formed during extraction was separated and analysed by HPLC and TLC. Fat extracts (acetone/hexane) were then concentrated to remove acetone and partitioned with acetonitrile (ACN). The ACN phase was analysed by HPLC and 2D TLC. After partitioning with acetonitrile, the hexane layer from Pyr-label milk fat still contained ~30% of TRR. This portion was analysed directly by TLC along with lipid standards. The hexane layer was saponified by refluxing for 3 hours with 1 M KOH in MeOH/H_2O (4:1, v/v). Post saponification, the extract was partitioned with hexane, then acidified and partitioned again with dichloromethane (DCM). The DCM portion was analysed by TLC.

Liver, kidney and muscle samples were extracted twice with acetonitrile/water (1:1, v/v) then once with acetonitrile. The organic extracts were separated from solids by centrifugation, concentrated and analysed by HPLC and 2D-TLC. PES were treated with KOH (0.1 M, 1 hr then 24% for 24 hours) then treated with acid (6 N HCl, 2 hours). The acid treated extract was partitioned with hexane or ethyl acetate and the aqueous portion analysed by HPLC.

Fat samples were extracted twice with acetone/hexane (1:4, v/v), then acetone. The organic extracts were separated from solids by centrifugation and the fat was extracted with acetonitrile (2 ×). The ^{14}C content of each combined extract was determined by LSC. A composite was made of the two extracts where acetonitrile extracts constituted a significant amount of residue (> 0.01 ppm, or 10% TRR). Extracts were concentrated to remove acetone and acetonitrile where applicable and the concentrated samples were partitioned/re-extracted with acetonitrile (3×). Acetonitrile layers were

analysed by HPLC and 2D TLC. Hexane layers (Pyr-label) were saponified with 1 M KOH in MeOH/H_2O (4:1, v/v) by refluxing for 3 hr. Saponified extracts were acidified and partitioned with dichloromethane, then analysed by TLC with oleic acid as a reference standard. Radiolabelled residues were very low in proportion to total mass and could not be separated. In addition, these residues appeared to have the same properties and Rf as oleic acid.

Subcutaneous fat samples formed a separate aqueous layer upon extraction. The aqueous layer was separated from the acetone/hexane extract. Aqueous layers were analysed separately by HPLC and 2D TLC.

Metabolite characterisation and confirmation was achieved by HPLC and TLC against reference standards.

Extractability of milk and fat with acetone/hexane and acetone was good at > 90% TRR while extractability of kidney, liver and muscle tissues with acetonitrile/H_2O and acetonitrile was lower but also good at > 67% TRR (Tables 33 and 34).

Parent pyrifluquinazon was not detected in any tissue or in milk.

The major free metabolites in both skim milk and milk fat were 1H-iminooxide (IV-04) (47.6–79.9% TRR) and 1H-oxide (IV-03) (1.8–8.4% TRR). Nicotinic acid N-oxide (11.4–22.3% TRR) was also present in Pyr-label milk, and quinazolinedione (IV-203) (8.4–19.5% TRR) in Qn-label milk. Aminoquinazolinone-N-Ac (IV-208) (3.8% TRR) was only found in Qn-label milk fat. Lipid conjugates of metabolites contributed 27.9 and 2.2% of the TRR in milk fat (Pyr- and Qn-labels respectively) and showed similar properties to fatty acids after saponification (17.2% TRR for Pyr-label).

The major residues in liver from the Pyr-label experiment were nicotinamide (IV-404) (67.7% TRR), nicotinic acid (IV-403) (1.9% TRR) and unknown 1, that was also found in Qn-label liver (15.3–43.4% TRR). Mass spectrometry of unknown 1 suggested it was comprised of glucuronides of 1H (IV-01), 4-oxo (IV-15) and 1H-4-oxo-imino-oxide (IV-04). Other residues found in liver consisted of 1H (IV-01), lH-4-oxo (IV-15), and quinazolinedione (IV-203), which is unique to the Qn-label (8.4% TRR). Qn-label liver also contained a small amount of residue (3.9% TRR), which had properties similar to fatty acids.

The major residues in kidney were similar to those of liver. Nicotinamide (IV-404) (1.791 mg eq/kg, 74.0% TRR) and methyl nicotinamide (IV-405) (4.1% TRR) were the major residues for the Pyr- label. The same glucuronide mixture that was found in liver was also present in kidney (7.2–16.7% TRR), as well as 1H (IV-01) (1.3–12.7% TRR) and lH-oxide (IV-03) (1.9–10.0% TRR). Quinazolinedione (IV-203) (30.8% TRR), and aminoquinazolinone N-Ac (IV-208) (8.0% TRR) were also present as the major residues from the Qn-label. Qn-label kidney also contained a small amount of residue (3.8% TRR) that had properties similar to fatty acids.

The major residue in Pyr-label muscle was nicotinamide (IV-404) (91.5–93.9% TRR). Quinazolinedione (IV-203) (51.4–57.3% TRR) and aminoquinazolinone-N-Ac (IV-208) (11.6–15.3% TRR) were the major residues identified in the Qn-label muscles, along with lower levels of 1H-oxide (IV-03), 1H (IV-01), and 1H-4-oxo (IV-15). Qn-label muscle also contained a small amount of residue (1.5–4.8% TRR), which was hydrolysed to fatty acids.

The major free metabolite in Pyr-label subcutaneous, omental and renal fat was nicotinamide (IV-404) (45.6–79.4% TRR). Lipid conjugates of metabolites contributed to 17.6–37.6% of the TRR in fat. Base saponification released residues that showed similar properties to fatty acids. The major free metabolites in Qn-label fat were quinazolinedione (IV-203) (53.1–58.2% TRR) and aminoquinazolinone-N-Ac (IV-208) (6.1–10.3% TRR). The hexane phase after partitioning with acetonitrile (tentatively assigned lipid conjugates of metabolites) contributed to 4.1–8.5% of the TRR in fat.

Table 33 Characterization and identification of residues in milk and tissues from Pyr-label experiment

	Skim milk	Milk fat	Fat – subcut.	Fat-omental	Fat-renal
Pyr-label					
TRR (mg equiv/kg)	0.349	0.720	0.312	0.125	0.171
		%TRR			
Solvent extracted (acetone/hexane, acetone)	**90.8**	**93.6**	**94.6**	**94.4**	**91.8**
Aqueous layer		**48.9**	**52.9**	**-**	**-**
nicotinamide (IV-404)	*1.1*	*-*	*52.2*	*-*	
nicotinic acid (IV-403)	*4.0*	*-*	*-*	*-*	*-*
nicotinic acid-N-oxide	*22.3*	*11.4*	*-*	*-*	*-*
methyl nicotinamide (IV-405)	*0.9*	*-*	*-*	*-*	*-*
1H-oxide (IV-03)	*3.7*	*1.8*	*-*	*-*	*-*
1H-imino-oxide (IV-04)	*53.3*	*34.2*	*-*	*-*	*-*
Unidentified	*5.4 (max 1.4)*	*1.5 (max < 1.0)*	*0.7 (max 0.3)*		
Acetone/hexane layer		**44.7**	**41.7**	**78.4**	**84.8**
Partition into ACN-ACN phase		*16.8*	*27.2*	*50.4*[a]	*50.3*
nicotinamide (IV-404)			*27.2*	*45.6*	*48.0*
1H-imino-oxide (IV-04)		*13.5*	*-*		
Partition into ACN-Hexane phase		*27.9*	*17.6*	*37.6*	*34.5*
Associated fatty acids		*17.2*	*12.5*	*26.4*	*26.9*
Solvent extracted (MeOH)				**4.0**	**4.1**
Unextracted by solvent	**9.2**	**6.4**	**5.4**	**8.0**	**11.1**
0.1N KOH	*NA*	*NA*	*NA*	*2.4*[b]	*2.9*[b]
24% KOH	*NA*	*NA*	*NA*	*NA*	*NA*

[a] 40.8%TRR ACN phase after partition + 9.6 ACN extract

[b] 1M KOH in MeOH/H_2O (4:1)

Milk fat – TLC of the hexane phase indicated the radioactivity was associated with triglycerides which when saponified was shown to be associated with natural fatty acids

Subcutaneous fat – the hexane phase from the combined acetone/hexane and ACN extracts (17.6% TRR) was saponified and partitioned with hexane (1.6% TRR basic hexane phase, 12.5% TRR acidic CH_2Cl_2 phase (fatty acids, same R_f as oleic acid), 3.5% TRR aqueous phase).

Omental fat – the hexane phase from the combined acetone/hexane and ACN extracts (37.6% TRR) was saponified and partitioned with hexane (2.4% TRR basic hexane phase, 26.4% TRR acidic CH_2Cl_2 phase (fatty acids, same R_f as oleic acid), 8.8% TRR aqueous phase). The PES were further extracted with MeOH (4.0% TRR) followed by 1 M KOH in MeOH/H_2O (4:1) which released an additional 2.4% TRR.

Renal fat – the hexane phase from the combined acetone/hexane and ACN extracts (34.5% TRR) was saponified and partitioned with hexane (0% TRR basic hexane phase, 26.9% TRR acidic CH_2Cl_2 phase (fatty acids, same R_f as oleic acid), 7.6% TRR aqueous phase). The PES were further extracted with MeOH (4.0% TRR) followed by 1 M KOH in MeOH/H_2O (4:1) which released an additional 2.9% TRR.

Table 33 cont. Characterization and identification of residues in milk and tissues from Pyr-label experiment

	Muscle-flank	Muscle-loin	Kidney	Liver
Pyr-label				
TRR (mg equiv/kg)	0.481	0.560	2.42	14.402
Solvent extracted (ACN/H_2O, ACN)	**94.8**	**95.7**	**93.6**	**87.9**
nicotinamide (IV-404)	*91.5*	*93.9*	*74.0*	*67.7*
nicotinic acid (IV-403)	-	-	-	*1.9*
methyl nicotinamide (IV-405)	-	-	*4.1*	-
1H (IV-01)	-	-	*1.3*	*1.4*[b]
1H-4-oxo (IV-15)	-	-	*0.4*	*With 1H*
1H-oxide (IV-03)	-	-	*1.9*	*0.4*
Glucuronide mixture [a]	-	-	*7.2*	*15.3*
Unidentified	*3.3 (max 2.7)*	*1.8 (max 1.6)*	*4.7 (max 0.3)*	*1.2 (max 0.4)*
Unextracted by solvent	**5.2**	**4.3**	**6.4**	**12.1**
0.1N KOH	*NA*	*NA*	*NA*	*1.7*
24% KOH	*NA*	*NA*	*NA*	*8.8*

[a] LC-MS suggested a mixture of three glucuronides mostly IV-01 and IV-15 with minor amounts of IV-04

Liver PES solubilised by KOH was partitioned with EtOAc, further 0.4% TRR 1H (IV-01) and 1H-4-oxo (IV-15) combined.

[b] IV-01 and IV-15 are not resolved

Table 34 Characterization and identification of residues in milk and tissues from Qn-label experiment

	Skim milk	Milk fat	Fat-subcut	Fat-omental	Fat-renal
Qn-label					
TRR (mg equiv/kg)	0.763	1.571	0.194	0.208	0.212
Solvent Extracted (acetone/hexane, acetone)	**98.8**	**95.8**	**92.3**	**93.3**	**93.4**
Aqueous layer		**51.9**	**10.3**		
quinazolinedione (IV-203)	*8.4*	*3.4*	*5.2*		
aminoquinazolinone N-Ac (IV-208)	-	-	*2.1*		
1H (IV-01)	-	*0.4*	*1.5*		
1H-4-oxo (IV-15)	*1.6*	-	-		
8-OH-quinazolinedione (IV-211)	-	-	*0.5*		
1H-oxide (IV-03)	*8.4*	*2*	-		
1H-imino-oxide (IV-04)	*79.9*	*44.9*	-		
Unidentified	*0.5 (max <1.0)*	*1.2 (max 0.6)*	*1 (max 0.5)*		
Acetone/hexane layer		**43.9**	**80.9**	**91.3**	**91**
Partition with ACN-ACN phase		41.8	76.8	83.7	82.5
quinazolinedione (IV-203)		*16.1*	*47.9*	*58.2*	*56.1*
aminoquinazolinone N-Ac (IV-208)		*3.8*	*8.2*	*6.7*	*6.1*
anthranilic acid (IV-303)					*1.9*
1H-imino-oxide (IV-04)		*19.6*			
1H-oxide (IV-03)		*0.6*			
1H (IV-01)		*0.6*	*1.5*	*1.9*	
1H-N-Ac (IV-17)	-	-	-	*4.3*	-
Unidentified		*3.1 (max 0.6)*	*19.2 (max 4.1)*	*12.6 (max 5.8)*	*18.4 (max 5.2)*
Partition with ACN-Hexane phase		2.2	4.1	7.7	8.5
Extracted ACN			**1**	**1.9**	**2.4**
Unextracted by solvent	**1.2**	**4.2**	**7.7**	**6.7**	**6.6**
0.1N KOH	*NA*	*NA*	*NA*	*NA*	*NA*
24% KOH	*NA*	*NA*	*NA*	*NA*	*NA*

Table 34 cont. Characterization and identification of residues in milk and tissues from Qn-label experiment

	Muscle – flank	Muscle-loin	Kidney	Liver
Qn-label				
TRR (mg equiv/kg)	0.146	0.131	0.812	5.187
				%TRR
Extracted (ACN/H_2O, ACN)	**84.9**	**87.8**	**84.4**	**67.5**
quinazolinedione (IV-203)	*51.4*	*57.3*	*30.8*	*8.4*
aminoquinazolinone N-Ac (IV-208)	*11.6*	*15.3*	*8.0*	*1.7*
1H (IV-01)	*8.2*[A]	*4.6* [a]	*12.7*	*1.1*
1H-4-oxo (IV-15)	*With 1H*	*With 1H*	*0.1*	*4.0*
1H-oxide (IV-03)	*3.4*	*3.1*	*10.0*	*1.8*
Glucuronide mixture (unknown 1)	*-*	*-*	*16.7*	*43.4*
Unidentified	*10.3 (max 2.7)*	*7.5 (max 3.1)*	*6.1 (max 1.6)*	*7.1 (max 0.8)*
Unextracted by solvent	**15.1**	**12.2**	**15.6**	**32.5**
0.1N KOH	*2.7*	*2.3*	*2.0*	*1.5*
24% KOH	*12.3*	*9.9*	*13.2*	*29.4*

Flank muscle PES solubilised by KOH (0.1N KOH + 24% KOH) was refluxed in 6M HCl for 2 hr and partitioned with hexane, 4.8% TRR into hexane (fatty acids) and 10.3%TRR into aqueous phase. The HPLC of the aqueous phase resolved 3 fractions (likely multicomponent), the maximum individual fraction comprising 2.7% TRR.

Loin muscle PES solubilised by KOH (0.1N KOH + 24% KOH) was refluxed in 6M HCl for 2 hr and partitioned with hexane, 1.5% TRR into hexane (fatty acids) and 10.7%TRR into aqueous phase. The HPLC of the aqueous phase resolved 3 fractions (likely multicomponent), the maximum individual fraction comprising 9.2% TRR.

Kidney PES solubilised by KOH (0.1N KOH + 24% KOH) was refluxed in 6M HCl for 2 hr and partitioned with hexane, 3.8% TRR into hexane (fatty acids) and 11.39%TRR into aqueous phase. The HPLC of the aqueous phase resolved 4 fractions (likely multicomponent), the maximum individual fraction comprising 8.1% TRR.

Liver PES solubilised by KOH (0.1N KOH + 24% KOH) was refluxed in 6M HCl for 2 hr and partitioned with hexane, 3.9% TRR into hexane (fatty acids) and 26.9%TRR into aqueous phase. The HPLC of the aqueous phase resolved 7 fractions, the maximum individual fraction was a broad (likely multicomponent) fraction comprising 19.7% TRR.

[a] IV-01 and IV-15 are not resolved

The glucuronide mixture (unknown 1) was investigated further in a separate study (Marin 2012 A-29022).

Separate Qn-label experiment liver and kidney solvent extracts were subject to a variety of efforts to hydrolyse conjugates.

Treatment of liver extracts with 2N HCl (40 °C), 10N H_2SO_4 (100 °C) and 2N NaOH (50 °C) did not release additional metabolites while incubation with 4N NaOH (50 °C) led to decomposition to a complex mixture of degradates. However, incubation with β-D-glucuronidase (Type IX from *E. coli*) was successful. Analysis by 2-D TLC revealed increases in IV-01, IV-15 and IV-203 following enzymatic digestion and a corresponding decrease in material at the origin (Table 35). The glucuronide conjugates (Unknown 1) in liver and kidney comprise mainly conjugates of IV-01 with small amounts of IV-15 and IV-203.

Table 35 Hydrolysis of Qn-label experiment liver and kidney extracts with β-D-glucuronidase

Component	Residue (mg equiv/kg)			
	Liver		Kidney	
	Before hydrolysis	After hydrolysis	Before hydrolysis	After hydrolysis
IV-01	0.230	1.284	0.021	0.103
IV-15	0.036	0.192	0.002	0.010
IV-203	0.675	0.706	0.268	0.250
Origin	1.943	0.114	0.135	0

In summary, the main components of the ^{14}C residues in goats are nicotinamide (IV-404) in muscle, fat, kidney and liver, quinazolinedione (IV-203) in milk fat, muscle, fat, kidney and liver,

aminoquinazolinone-N-Ac (IV-208) in muscle, fat and kidney, 1H (IV-01) in liver and kidney, 1H-imino-oxide (IV-04) in skim milk and milk fat and nicotinic acid N-oxide in skim milk and milk fat.

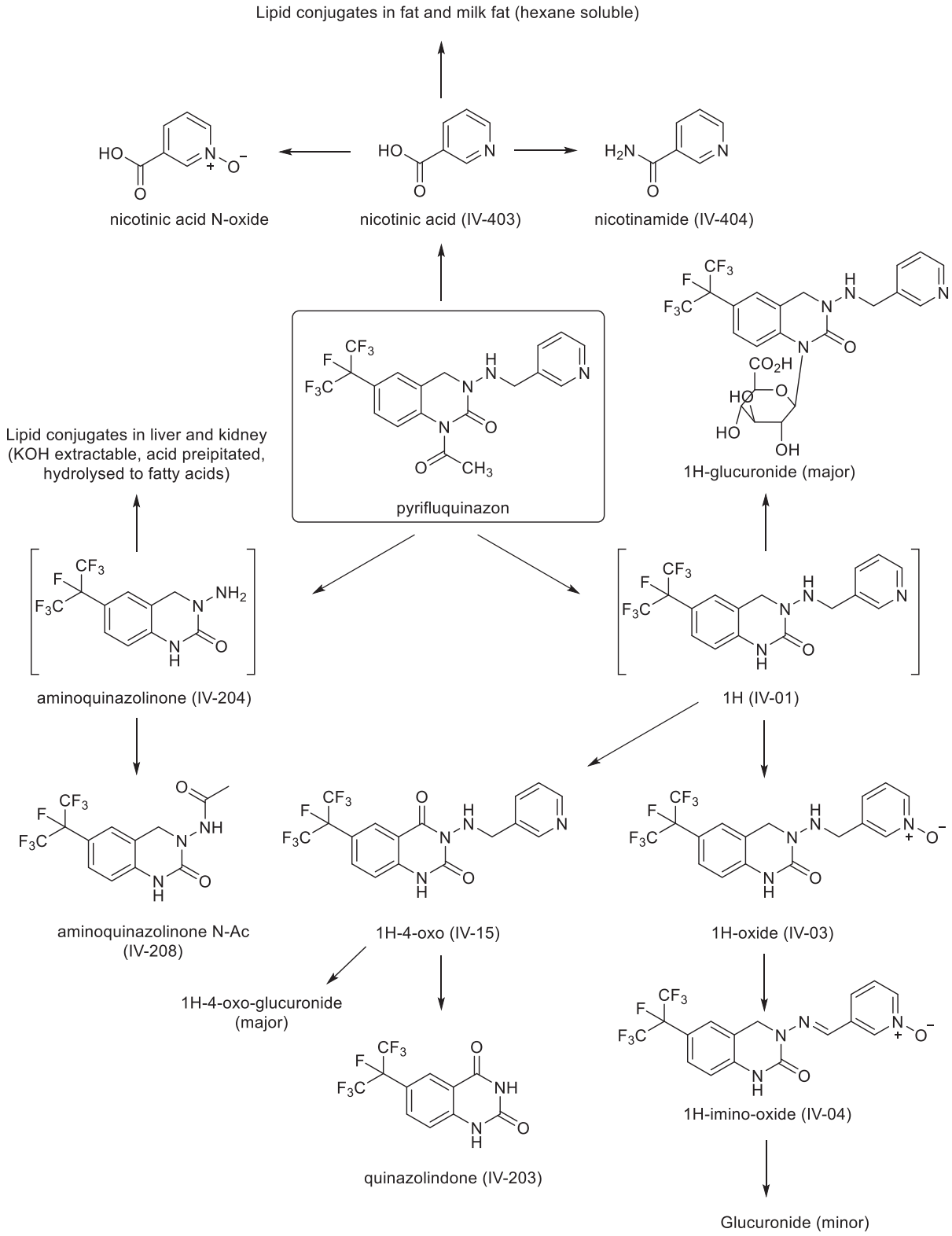


Figure 6 Metabolites of pyrifluquinazon identified in tissues and milk of lactating goats.

Laying hen

Quinstad and LaMar (2009 R-29059) studied the metabolism of pyrifluquinazon in laying hens. Hens (1.4-2.0 kg bw) were dosed orally *via* intubation, once a day for a total of seven days, with [quinazolinone-phenyl-U-^{14}C]- or [pyridine-2,6-^{14}C]-pyrifluquinazon at doses equivalent to 14 ppm in the diet (0.8 mg/kg bw). Feed consumption averaged 92 (Pyr experiment) and 91 (Qn experiment) g/d. Average laying efficiency during the dosing period was 96 (Pyr-label) and 91 (Qn-label) %. Egg samples were collected twice a day in the morning and evening; excreta samples were collected daily. Hens were sacrificed 21 to 22 hours after the final dose, and samples of fat, thigh and breast muscle, liver, and gastrointestinal tract and contents were collected. Metabolite characterisation and confirmation was achieved by HPLC and TLC against reference standards.

Excretion of pyrifluquinazon was fast, with 63.4% AD (Pyr-label) and 77.0% AD (Qn-label) found in the excreta by 20–22 hours after the last dose (Table 36). A significant portion of the administered radioactivity was excreted in eggs (0.86–3.6% AD) or found in tissues (3.6–11.1% AD).

Table 36 Recovery of administered dose in eggs, tissues, and excreta of laying hens following dosing for seven consecutive days (seven doses) with [^{14}C]-pyrifluquinazon [a] (Quinstad and LaMar 2009 R-29059)

Sample	Pyr-label		Qn-label	
	% AD	Residue (mg equiv/kg)	% AD	Residue (mg equiv/kg)
Tissues	**11.1**		**3.6**	
Liver	*3.7*	*6.374*	*1.3*	*2.255*
Fat	*0.1*	*0.163*	*0.2*	*0.382*
Muscle	*7.3*	*1.033*	*2.1*	*0.300*
Eggs	**0.86**		**3.57**	
Excreta	**63.4**		**77.0**	
GIT	**3.5**		**2.0**	
Total	**78.9**		**86.2**	

[a] Assumed muscle 35% BW (Gregory and Robins 1998)

Gregory N.G.; Robins J.K. 1998: A body condition scoring system for layer hens. New Zealand Journal of Agricultural Research 41: 555-559

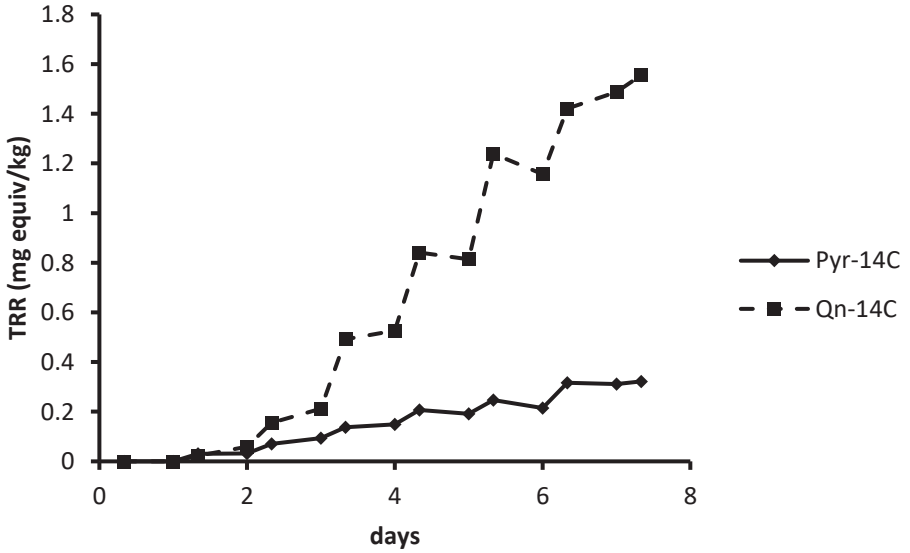


Figure 7 Residues in eggs following dosing with ^{14}C-pyrifluquinazon, Pyr- and Qn-label

Residues in eggs from both labels continued to rise during the course of the experiment, consistent with the physiology of egg formation (Figure 7).

A range of extraction schemes were used to further characterise residues in eggs and tissues.

Eggs: were extracted twice with acetonitrile/water (1:1, v/v) and then once with acetonitrile. The organic extracts were separated from solids by centrifugation, concentrated and analysed by HPLC and 2D-TLC. The remaining PES were treated with KOH (0.1M, 1 hour then 24% for 24 hours). A composite was made from the KOH extracts, which were acidified, and then partitioned with ethyl acetate. A percentage of the ethyl acetate phase was concentrated to dryness, and re-partitioned with hexane and water. The aqueous phase was analysed by HPLC. Aqueous phases from Pyr-label experiment egg KOH extracts were concentrated to dryness, and then re-dissolved in acetonitrile, methanol, then water, keeping all three solvents separate. Acetonitrile and methanol phases were further analysed by TLC.

Liver samples were extracted twice with acetonitrile/water (1:1) then once with acetonitrile. The organic extracts were separated from solids by centrifugation, concentrated and analysed by HPLC and 2D-TLC. The remaining PES were treated with KOH (0.1M, 1 hour then 24% for 24 hours). The liver PES from the Qn-label experiment was additionally treated using acid hydrolysis (6 N HCl, 3 hours). A composite sample from KOH and HCl extracts was acidified and the precipitate which formed separated and re-extracted with ethyl acetate. The ethyl acetate extract was then used for partitioning of the composite extract. A percentage of the ethyl acetate phase was then concentrated to dryness, combined with the same proportion of aqueous phase, and re-partitioned with hexane. The aqueous phase was then analysed by HPLC. The hexane phase was analysed by TLC.

Breast and thigh muscle samples were extracted separately. Portions of breast and thigh muscle samples were extracted twice with acetonitrile/water (1:1, v/v) and then once with acetonitrile. The organic extracts were separated from solids by centrifugation, concentrated and analysed by HPLC and 2D-TLC. The PES from the Pyr-label experiment was treated using base hydrolysis (0.1M, 1 hour then 24% for 24 hours). A precipitate formed upon acidification of the KOH extracts. The precipitate was separated by centrifugation, and then re-extracted with water and ethyl acetate. The water and ethyl acetate extracts were then used for partitioning of the acidified KOH extracts. The aqueous phase was then analysed by HPLC and TLC. Aqueous phases from Pyr-^{14}C labelled muscle KOH extracts were also concentrated to dryness, and then re-dissolved in acetonitrile, methanol (MeOH), then water, keeping all three solvents separate. MeOH phases were further analysed by TLC.

Fat samples were extracted with acetone/hexane (1:4, v/v), then acetone. The organic extracts were separated from solids by centrifugation. Acetone was removed from the extracts which were re-extracted three times with acetonitrile. Acetonitrile extracts were analysed by HPLC and 2D-TLC. The hexane phase from the Pyr-label experiment was saponified with 1 M KOH in MeOH/H_2O (4:1, v/v) by refluxing for 3 hours then partitioned with hexane. The aqueous phase was then acidified, and partitioned with DCM and the DCM phase analysed by TLC. The PES was further extracted with acetonitrile, then MeOH, then 1M KOH in MeOH/H_2O (4:1, v/v).

Extractability with solvents was good for muscle and fat (> 82% TRR) but lower for liver (62–88% TRR) and eggs (43–89% TRR).

Parent pyrifluquinazon was not detected in any tissue or egg samples.

The major components of the ^{14}C residue were nicotinamide (IV-404) (eggs 24.6% TRR, liver 81.8% TRR, muscle 72.6–81.8% TRR, fat 64.4% TRR), quinazolindione (IV-203) (eggs 32.3% TRR, liver 24.9% TRR, muscle 37.5–48.3% TRR, fat 74.9% TRR) and aminoquinazolinone N-Ac (IV-208) (eggs 49.7% TRR, liver 14.6% TRR, muscle 27.3–35.4% TRR, fat 18.1% TRR).

A portion of the ^{14}C residue in eggs and fat was associated with fatty acids (eggs 2.9–26.9% TRR; fat 16.8% TRR; liver 7.2% TRR).

Table 37 Characterization and identification of residues in eggs and tissues from Pyr-label experiment (mean values) (Quinstad and LaMar 2009 R-29059)

	Eggs	Liver	Breast muscle	Thigh muscle	Fat
TRR (mg equiv/kg)	0.309	6.257	0.926	1.213	0.137
		%TRR			
Solvent Extract [a]	**43.4**	**88.0**	**82.5**	**87.6**	**86.1**
Partition acetonitrile phase	NA	NA	NA	NA	*65.7*
1H-4-oxo (IV15)	*3.2*	*4.1*			
Nicotinic acid (IV-403)			*1.5*		
Nicotinamide (IV-404)	*24.6*	*81.8*	*72.6*	*74.2*	*64.4*
Unidentified	*15.6 (n=8; max 4.9)*	*2.1 (n=4; max 0.8)*	*8.4 (n=4; max 2.8)*	*13.4 (n=5; max 5.2)*	*1.3 (n=1)*
Partition hexane phase	NA	NA	NA	NA	*20.4*
Solvent Extract (ACN)					**1.5**
Solvent Extract (MeOH)					**5.1**
Unextracted by solvent	**56.6**	**12.0**	**17.5**	**12.4**	**13.9**
0.1 M KOH		1.3			2.9[b]
24% KOH	56.0	7.0	17.2	12.2	

[a] extraction solvents: Eggs, liver, muscle: ACN/H_2O, ACN; fat, acetone/hexane and acetone

[b] 0.1M KOH in MeOH/H_2O (4:1 v/v)

Eggs: combined solubilised material following KOH treatments (56%TRR) were acidified and partitioned with ethyl acetate, 26.9% TRR was in the ethyl acetate (tentative assigned fatty acids) and 29.1% TRR in the aqueous phase and comprised two fractions on HPLC analysis.

Breast muscle: combined solubilised material following KOH treatments (17.2%TRR) were acidified and partitioned with ethyl acetate, 0.5% TRR was in the ethyl acetate and 16.6% TRR in the aqueous phase and comprised two fractions on HPLC analysis.

Thigh muscle: combined solubilised material following KOH treatments (12.2%TRR) were acidified and partitioned with ethyl acetate, 0.6% TRR was in the ethyl acetate and 11.6% TRR in the aqueous phase and comprised three fractions on HPLC analysis.

Fat: Solvent was removed from combined acetone/hexane and acetone extracts were partitioned against ACN, 65.7% TRR was in the ACN phase and 20.4% TRR in hexane. The hexane phase was saponified with KOH and partitioned into CH_2Cl_2 (16.8% TRR) (associated fatty acids) with 3.6% remaining in the aqueous phase.

Table 38 Characterization and identification of residues in eggs and tissues from Qn-label experiment (mean values) (Quinstad and LaMar 2009 R-29059)

	Eggs	Liver	Breast muscle	Thigh muscle	Fat
TRR (mg equiv/kg)	0.309	6.257	0.926	1.213	0.137
		%TRR			
Solvent extract [a]	**88.5**	**61.6**	**91.3**	**91.8**	**97.8**
Partition acetonitrile phase					95.9
Quinazolinedione (IV-203)	*32.2*	*24.9*	*48.3*	*37.5*	*74.9*
Aminoquinazolinone N-Ac (IV-208)	*49.7*	*14.6*	*27.3*	*35.4*	*18.1*
Anthranilic acid (IV-303)					*1.3*
1H-oxide (IV-03)		*1.5*			
1H-4-oxo (IV-15)		*10.5*			
unidentified	*6.6 (n=5; max 2.2)*	*10.1 (n=4; max 8.6)*	*15.7 (n=6; max 9.8)*	*18.9 (n=5; max 11.9)*	*0*
Partition hexane phase					1.9
Unextracted	**11.5**	**38.4**	**8.7**	**8.2**	**2.2**
0.1 M KOH		1.4			
24% KOH	11.1	17.0	-	-	
6N HCl		3.9			

[a] extraction solvents: Eggs, liver, muscle: ACN/H_2O, ACN; fat, acetone/hexane and acetone

[b] 0.1M KOH in MeOH/H_2O (4:1 v/v)

Liver: combined solubilised material following 0.1M KOH, 24% KOH and 6N HCl treatments (22.2% TRR) were partitioned with hexane, 8.5% TRR precipitated on acidification, 7.2% TRR was in the hexane phase (fatty acids) and 6.5% TRR in the aqueous phase and comprised three fractions on HPLC analysis.

Eggs: combined solubilised material following KOH treatments (11.1%TRR) were acidified and partitioned with ethyl

acetate, 2.9% TRR was in the ethyl acetate (tentative assigned fatty acids) and 8.2% TRR in the aqueous phase and comprised quinazolinedione (IV-203) 2.4% TRR and four other unidentified fractions on HPLC analysis.

HPLC analysis of an extract of excreta (day 8) showed possible nicotinamide (IV-404) from the Pyr-label experiment and aminoquinazolinone-N-Ac (IV-208) from the Qn-label, but in general the profile of residues was dissimilar compared to tissues.

Extracts from ^{14}C labelled tissues were re-analysed by HPLC in the same manner as initial analysis approximately 209–216 days following animal sacrifice. No major changes in ^{14}C residue composition were observed with the exception of Qn-label experiment breast muscle. A small previously unidentified peak at retention time 11.8 min (0.028 mg/kg, 9.8% TRR) was no longer present and aminoquinazolinone-N-Ac (IV-208) had increased slightly (approximately the same difference).

In a similar fashion, extracts from ^{14}C labelled eggs were re-analysed by HPLC in the same manner as initial analysis approximately 209 days following animal sacrifice. No major changes in ^{14}C residue composition were observed for egg extracts from the Qn-label experiment. Pyr-label egg extracts which previously consisted mostly of nicotinamide (IV-404) (0.076 mg/kg, 24.6% TRR) had a much more diverse array of ^{14}C residues, most of which were observed following initial analysis at much lower levels.

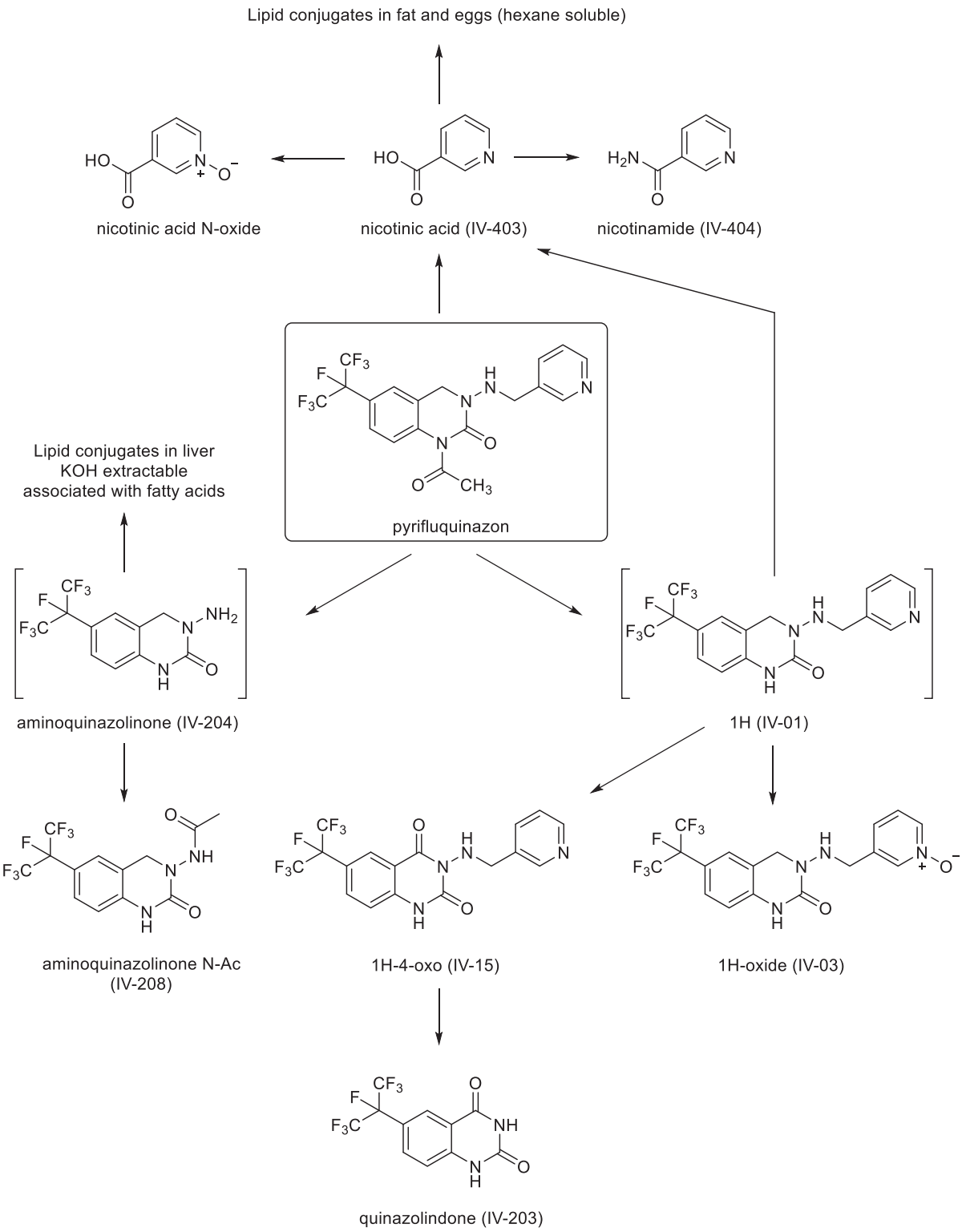


Figure 8 Metabolites of pyrifluquinazon identified in laying hen tissues and eggs

METHODS OF RESIDUE ANALYSIS

Analytical methods

The Meeting received descriptions and validation data for analytical methods for residues of pyrifluquinazon and 1H (IV-01) in plant matrices and pyrifluquinazon and IV-01 (liver, kidney), IV-03 (kidney), IV-04 (milk), IV-15 (liver, kidney), IV-203 (milk, liver, kidney, muscle, fat) and IV-208 (muscle, fat) in animal matrices. The methods are suitable for analysis of pyrifluquinazon and 1H (IV-01) in plant and pyrifluquinazon and metabolites in animal matrices.

Table 39 Overview of the methods for determination of pyrifluquinazon in crops

<table>
<tr><td></td><td></td><td>Method 188 rev.2 and rev.3 (A-29015) rev 4</td><td>Method 188 rev.2 and rev.3 (A-29013)</td></tr>
<tr><td rowspan="5">Extraction and clean-up</td><td>Analytes</td><td>Pyrifluquinazon, 1H (IV-01)</td><td>Pyrifluquinazon, 1H (IV-01)</td></tr>
<tr><td>Matrix</td><td>Almond hulls, almond nutmeat, apple, cotton gin by-products, cotton seed, cotton seed refined oil, cucumber, grape, head lettuce, orange, potato flakes, potato tubers, tomato</td><td>Cotton seed</td></tr>
<tr><td>Extraction</td><td>Note: all samples must be kept in the frozen state until addition of the extraction solvent.
Oils:
Pyrifluquinazon and 1H (IV-01) were extracted with acetonitrile: 0.1N HCl (4:1, v/v), the aqueous layer was retained and diluted with acetonitrile:0.1N HCl (4:1, v/v) and an aliquot filtered and further diluted with acetonitrile:buffer solution (50:50, v/v, pH4) and analysed directly by HPLC.
Other:
Pyrifluquinazon and 1H (IV-01) were extracted with acetonitrile:0.1N HCl (4:1, v/v) and centrifuged to separate supernatant and solids. Any remaining solids were re-extracted with acetonitrile:0.1N HCl (4:1, v/v), centrifuged and the supernatants combined. An aliquot of diluted extract was filtered and further diluted with acetonitrile:buffer solution (50:50, v/v, pH4) and analysed directly by HPLC.</td><td>Macerated un-delinted cotton seed samples (5 g), homogenized in the presence of dry ice, were extracted with 150 mL portions of acetonitrile: 0.1 N HCl in water (4:1,v/v), centrifuged and the supernatant was decanted into a 250 mL mixing cylinder through a glass funnel containing a loosely packed plug of glass wool. 50mL of acetonitrile: 0.1 N HCl in water (4:1, v/v) were added to extract residue and the samples were shaken by hand for 15 seconds and centrifuged and the supernatant decanted through the same glass wool and the extracts combined. The volume was adjusted with acetonitrile: 0.1 N HCl in water (4:1, v/v). An aliquot was transferred to a syringe and filtered through a 0.45µm PTFE filter into a glass test tube. An aliquot of 0.5 mL of the filtered extract was transferred into a glass test tube and the final volume adjusted with acetonitrile: buffer solution (50:50, v/v, pH 4).</td></tr>
<tr><td>Column</td><td>For extracts requiring further clean-up (potato tubers and cotton seed refined oil): an aliquot of the filtered diluted extract was purified by means of an Oasis® HLB solid phase extraction clean-up. The purified extract was concentrate, diluted with pH 4 buffer solution and analysed by HPLC</td><td></td></tr>
<tr><td>Eluent</td><td>Methanol</td><td></td></tr>
<tr><td rowspan="5">Chromatography</td><td>Type</td><td>HPLC</td><td>HPLC</td></tr>
<tr><td>Analytical column</td><td>Phenomenex Luna C18 (2)-HST, with 0.1% formic acid in water mobile phase</td><td>Phenomenex Luna C18 (2)-HST, with 0.1% formic acid in water mobile phase</td></tr>
<tr><td>Dimensions</td><td>100 mm×2.0 mm</td><td>100 mm×2.0 mm</td></tr>
<tr><td>Particle size</td><td>2.5 micron particle size</td><td>2.5 micron particle size</td></tr>
<tr><td>Mobile phase</td><td>A: 0.1% formic acid in water
B: 100% acetonitrile
<table>
<tr><td>Time (min)</td><td>%phase A</td><td>%phase B</td></tr>
<tr><td>0-1.0</td><td>75</td><td>25</td></tr>
<tr><td>7</td><td>28.3</td><td>71.7</td></tr>
<tr><td>7.51-9.5</td><td>0</td><td>100</td></tr>
</table></td><td>A: 0.1% formic acid in water
B: 100% acetonitrile
<table>
<tr><td>Time (min)</td><td>%phase A</td><td>%phase B</td></tr>
<tr><td>0-1.0</td><td>75</td><td>25</td></tr>
<tr><td>1.01-7</td><td>28.3</td><td>71.7</td></tr>
<tr><td>7.01-9.5</td><td>0</td><td>100</td></tr>
</table></td></tr>
</table>

		Method 188 rev.2 and rev.3 (A-29015) **rev 4**			Method 188 rev.2 and rev.3 (A-29013)		
		9.51-12.5	75	25	9.51-12.5	75	25
	Injection volume	10 µL			10 µL		
	Flow rate	250 µL/min			250 µL/min		
	Instrument	Shimadzu LC-20AD			Shimadzu LC-20AD		
Detection	Quantitative detection	MS/MS Pyrifluquinazon: m/z 465.2 → 423.2 (quantification) and m/z 465.2 → 106.9 (confirmation) 1H (IV-01): m/z 423.2 → 106.9 (quantification) and m/z 423.2 → 93.0 (confirmation)			MS/MS Pyrifluquinazon: m/z 465.2 → 423.2 (quantification) and m/z 465.2 → 106.9 (confirmation) 1H (IV-01): m/z 423.2 → 106.9 (quantification) and m/z 423.2 → 93.0 (confirmation)		
	LOQ	0.01 mg/kg			0.01 mg/kg		
	Whole method linearity (r^2)	0.02-1.0 ng/mL r≥0.990			0.02-1.0 ng/mL r≥0.990		

Table 39 continued

		Method R-29046	Method R-29049	Method R-29050
Extraction and clean-up	Analytes	Pyrifluquinazon, 1H (IV-01)	Pyrifluquinazon, 1H (IV-01)	Pyrifluquinazon, 1H (IV-01)
	Matrix	Tea leaves (dried)	Tea leaves	Tea leaves
	Extraction	Dried tea leaves were soaked in distilled water for 30 mins, acetonitrile added and the mixture mechanically shaken. The solution was suction filtered and the remaining solids and flask washed with acetonitrile:distilled water (4:1, v/v). The rinsates were combined. An aliquot was cleaned up with a Bond Elut C18 cartridge column. The eluate was diluted with distilled water and analysed by LC-MS.	Dried tea leaves were soaked in distilled water for 2 hours, acetonitrile added and the mixture mechanically shaken. The solution was suction filtered and the remaining solids and flask washed with acetonitrile. The rinsates were combined. An aliquot was cleaned up with a polymer based mini column. Eluting with water:acetonitrile (2:8, v/v). The eluate was concentrated in vacuo and reconstituted in water:acetonitrile:formic acid (600:400:1, v/v/v) and analysed by LC-MS.	Dried tea leaves were soaked in distilled water for 30 min, acetonitrile added and the mixture mechanically shaken. The solution was suction filtered and the remaining solids and flask washed with acetonitrile:water (4:1, v/v). The rinsates were combined. An aliquot was cleaned up with a ODS cartridge column, eluting with water:acetonitrile (4:1, v/v). The eluate was concentrated in vacuo and reconstituted in acetonitrile:ultrapure water (2:3, v/v) and analysed by LC-MS.
Chromatography	Type	LC	LC	LC
	Analytical column	Cadenza CD-C18 column	Atlantis dC18 (Waters)	Cadenza CD-C18 column
	Dimensions	75×2 mm id	150×2.1 mm id	75×2 mm id
	Particle size	3 µm	5 µm	3 µm
	Injection volume	1 µL	5 µL	1 µL
	Mobile phase	50% acetonitrile/water containing 1 mM ammonium formate	5 mmol/L ammonium acetate/acetonitrile (52:48 v/v)	Ultra pure water/acetonitrile/formic acid (65:35:0.1 v/v/v)
	Flow rate	0.2 mL/min	0.2 mL/min	0.2 mL/min
	Instrument	Agilent 1100 with JMS-7000 mass spectrometer	Agilent 1100 LC-MSD	Agilent 1100 LC-MSD
Detection	Quantitative detection	MS Pyrifluquinazon: m/z 465 (retention time ca. 4.3 mins) 1H (IV-01): m/z 423 (retention time ca. 3 mins)	MS ESI/SIM detector Pyrifluquinazon: m/z 465.1 (retention time 12.7 min) 1H (IV-01): m/z 423.1 (retention time 9.0 min)	MS ESI/SIM detector Pyrifluquinazon: m/z 465 1H (IV-01): m/z 423
	LOQ	0.05 mg/kg	0.05 mg/kg	0.05 mg/kg
	Whole method linearity (r^2)	0.0005–0.1 µg/mL, r^2≥ 0.998	0.0005–0.2 µg/mL, r≥ 0.99	0.0005–0.03 µg/mL, r^2≥ 0.99

Table 39 continued

		Method R-29051	Method R-29108
Extraction and clean-up	Analytes	Pyrifluquinazon, 1H (IV-01)	Pyrifluquinazon, IV-203
	Matrix	Tea infusion	Radish roots, lettuce leaves, sorghum forage, sorghum grain, sorghum stover
	Extraction	Dried tea leaves were soaked in boiling water for 5 min and the solution suction filtered. The filtrate was allowed to cool and then acetonitrile was added. An aliquot was cleaned up with a PLS2 cartridge column, eluting with acetonitrile:distilled water (4:1, v/v). The eluate was concentrated in vacuo and reconstituted in acetonitrile:ultrapure water (2:3, v/v) and analysed by LC-MS.	Note: samples are homogenized in the presence of dry ice. Residues of pyrifluquinazon and IV-203 were extracted from the sample using acetonitrile:water (1:1, v/v) 2× and then acetonitrile. Extracts were filtered or centrifuged and the supernatants combined. For radish roots, tops, lettuce and sorghum forage no further cleanup was required and an aliquot was diluted with acetonitrile:buffer solution (50:50, v/v, pH4) for HPLC analysis. Sorghum grain and stover samples were processed through a Strata-X SPE cleanup, extracts diluted with acetonitrile:buffer solution (50:50, v/v, pH 4) for HPLC analysis.
Chromatography	Type	LC	LC
	Analytical column	Cadenza CD-C18 column	Phenomenex Luna C18
	Dimensions	75 × 2 mm id	100 × 2 mm id
	Particle size	3 µm	2.5 µL
	Injection volume	1 µL	10 µL
	Mobile phase	Ultra pure water/acetonitrile/formic acid (65:35:0.1 v/v/v)	A: 0.1% formic acid in water B: acetonitrile Time (min) / %A / %B 0–0.5 / 90 / 10 1.0 / 75 / 25 3.5 / 55 / 45 9.0 / 40 / 60 9.51-11.5 / 0 / 100 11.51-14.51 / 90 / 10
	Flow rate	0.2 mL/min	0.25 mL/min
	Instrument	Agilent 1100 LC-MSD	Schimadzu LC-20AD with Applied Biosystems API 4000 MS/MS detector
Detection	Quantitative detection	MS ESI: Pyrifluquinazon: m/z 465 1H (IV-01): m/z 423	MS/MS At least two ion transitions were monitored for each analyte: Pyrifluquinazon: m/z 465.2 → 423.2 (quantification) and m/z 465.2 → 92.3 (confirmation) IV-203: m/z 329.0 → 309.0 (quantification) and m/z 329.0 → 240.0 and 329.0 → 289.0(confirmation)
	LOQ	0.05 mg/kg	0.01 mg/kg
	Whole method linearity (r^2)	0.0005–0.03 ng/mL $r^2 \geq 0.99$	0.02-1.0 ng/mL $r \geq 0.99$

Recovery and repeatability data for the determination of pyrifluquinazon residues in crops are presented in Table 40 for Method 188 rev2 and rev 3. Average recoveries ranged from 78 to 109%. The LOQ was 0.01 mg/kg. The %RSDs ranged from 0.8 to 12. Calibration curves over the range 0.02–1.0 ng/mL for each analyte demonstrated linearity with $r \geq 0.990$.

Table 40 Recovery data obtained during validation of Method 188 rev.2 (Clark 2017 A-29015) and rev.3 (Westburg 2009 A-29016)

Commodity	Analyte	Fortification level (mg/kg)	n	Range of Recoveries (%)	Mean Recovery (%)	RSD (%)
Almond hulls	Pyrifluquinazon	0.01	5	82-93	86	6.7
		5.0	5	95-109	103	5.5
	1H (IV-01)	0.01	5	91-115	106	8.8
		5.0	5	94-108	100	7.2
Almond Nutmeats	Pyrifluquinazon	0.01	5	92-99	96	3.5
		5.0	5	99-109	102	3.8
	1H (IV-01)	0.01	5	79-105	91	12
		5.0	5	102-107	104	2.0
Apples	Pyrifluquinazon	0.01	5	91-102	97	4.4
		5.0	5	96-103	100	3.0
	1H (IV-01)	0.01	5	100-106	103	2.7
		5.0	5	104-110	106	2.1
Cotton Gin By-products	Pyrifluquinazon	0.01	5	75-87	83	5.8
		5.0	5	85-93	91	3.7
	1H (IV-01)	0.01	5	89-114	100	12
		5.0	5	88-90	89	0.9
Cottonseed	Pyrifluquinazon	0.01	5	94-104	98	4.4
		5.0	5	97-98	98	0.5
	1H (IV-01)	0.01	5	90-114	107	9.0
		5.0	5	97-108	102	4.7
Cottonseed Refined Oil	Pyrifluquinazon	0.01	5	86-96	91	4.4
		5.0	5	88-93	90	2.2
	1H (IV-01)	0.01	5	90-108	102	7.6
		5.0	5	88-100	93	4.8
Cucumbers	Pyrifluquinazon	0.01	5	79–91	83	6.2
		5.0	5	102-106	104	1.6
	1H (IV-01)	0.01	5	82-107	99	10
		5.0	5	97-109	105	5.2
Grapes	Pyrifluquinazon	0.01	5	92-104	98	4.9
		5.0	5	100-115	107	5.0
	1H (IV-01)	0.01	5	98-114	105	5.9
		5.0	5	94-118	105	8.2
Head Lettuce	Pyrifluquinazon	0.01	5	94-106	100	5.1
		5.0	5	100-102	101	0.9
	1H (IV-01)	0.01	5	94-111	104	7.6
		5.0	5	103-106	104	1.3
Oranges	Pyrifluquinazon	0.01	5	90-98	92	3.6
		5.0	5	98-108	103	4.0
	1H (IV-01)	0.01	5	99-114	109	5.9
		5.0	5	100-105	103	1.9
Potato Flakes	Pyrifluquinazon	0.01	5	96-105	100	4.0
		5.0	5	103-110	105	2.9
	1H (IV-01)	0.01	5	93-104	99	4.7
		5.0	5	97-105	101	2.9

Commodity	Analyte	Fortification level (mg/kg)	n	Range of Recoveries (%)	Mean Recovery (%)	RSD (%)
Potato Tubers	Pyrifluquinazon	0.01	5	74-84	78	5.2
		5.0	5	83-97	88	6.0
	1H (IV-01)	0.01	5	97-110	103	4.6
		5.0	5	94-103	99	3.9
Tomatoes	Pyrifluquinazon	0.01	5	85-95	91	4.2
		5.0	5	90-108	99	7.4
	1H (IV-01)	0.01	5	97-116	105	6.8
		5.0	5	88-101	95	5.5

Recovery and repeatability data for the determination of pyrifluquinazon residues in cotton seed are presented in Table 41 for an ILV study for method 188 rev2 (Boatwright 2017 A-29013). Average recoveries ranged from 104 to 113%. The LOQ was 0.01 mg/kg. The %RSDs ranged from 2 to 14.5. Calibration curves over the range 0.02-1.0 ng/mL for each analyte demonstrated linearity with $r \geq 0.990$.

Table 41 Recovery data for cotton seed obtained during validation of Method 188 rev.2 (Boatwright 2017 A-29013)

Commodity	Analyte	Fortification level (mg/kg)	n	Range of Recoveries (%)	Mean Recovery (%)	RSD (%)	Method	Reference
Cotton seed	Pyrifluquinazon	0.01	5	91-127	106	14.5	Meth-188, rev.2	A-29013
		5.0	5	106-111	108	2.0		
	1H (IV-01)	0.01	5	93-123	104	11.7		
		5.0	5	110-117	113	3.1		

Recovery and repeatability data for the determination of pyrifluquinazon residues in green tea are presented in Table 42 (trial reports R29046, R-29049, R-29050, R-29069). Average recoveries ranged from 77 to 115%. The LOQ was 0.05 mg/kg. The %RSDs ranged from 0.9–15.9. Calibration curves over the range 0.0005–0.03 µg/mL for each analyte demonstrated linearity with $r^2 \geq 0.99$.

Table 42 Recovery data for green tea (dry) (*R29046, R-29049, R-29050, R-29069*)

Commodity	Analyte	Fortification level (mg/kg)	n	Range of Recoveries (%)	Mean Recovery (%)	RSD (%)	Method	Reference
Dried tea leaves	Pyrifluquinazon	0.05	6	77-90	86	6.1	-	R-29046
		1.0	6	70-90	79	12.5		
		20	6	74-83	77	4.3		
	1H (IV-01)	0.05	6	94-114	104	7.3		
		1.0	6	70-99	86	15.9		
		20	6	74-82	79	4.3		
Dried tea Leaves	Pyrifluquinazon	0.05	6	82-91	87	3.5	-	R-29049
		20	6	91-93	92	0.9		
	1H (IV-01)	0.05	6	88-95	92	3.0		
		20	6	90-94	92	1.7		
Dried tea Leaves	Pyrifluquinazon	0.05	6	93-114	102	7.1	-	R-29050
		11	3	103-105	104	1.1		
		20	3	105-107	106	1.1		
	1H (IV-01)	0.05	6	111-119	115	2.6		
		11	3	94-96	95	1.2		
		20	3	102-105	104	1.5		

Commodity	Analyte	Fortification level (mg/kg)	n	Range of Recoveries (%)	Mean Recovery (%)	RSD (%)	Method	Reference
Dried tea leaves	Pyrifluquinazon	0.05	12	98-107	101	2.5	-	R-29069
		0.5	3	98-110	106	6.5		
		1.5	3	102-106	104	2.0		
		2.5	3	93-99	96	3.1		
		6.0	3	99-103	101	2.1		
	1H (IV-01)	0.05	12	99-119	110	6.4		
		0.5	3	107-120	114	5.8		
		1.5	3	89-100	95	5.9		
		5.0	6	100-108	103	2.9		

Recovery and repeatability data for the determination of pyrifluquinazon residues in green tea infusion are presented in Table 43 (R29051). Average recoveries ranged from 95 to 109%. The LOQ was 0.05 mg/kg. The %RSDs ranged from 3.0–6.3. Calibration curves over the range 0.0005–0.03 µg/mL for each analyte demonstrated linearity with $r^2 \geq 0.99$.

Table 43 Recovery data for green tea infusion (*R29051*)

Commodity	Analyte	Fortification level (mg/kg)	n	Range of Recoveries (%)	Mean Recovery (%)	RSD (%)	Method	Reference
Tea Infusion	Pyrifluquinazon	0.05	6	90-104	95	6.3	-	R-29051
		2.0	6	101-114	106	4.4		
	1H (IV-01)	0.05	6	99-115	109	5.8		
		2.0	6	99-107	102	3.0		

Recovery and repeatability data for the determination of pyrifluquinazon and IV-203 residues in radish, lettuce and sorghum are presented in Table 44 (R-29108). Average recoveries ranged from 81 to 114%. The LOQ was 0.01 mg/kg. The %RSDs ranged from 1.3-16.5. Calibration curves over the range 0.02-1.0 ng/mL for each analyte demonstrated linearity with $r \geq 0.990$.

Table 44 Recovery data for pyrifluquinazon and IV-203 in rotational crops (R-29108)

Commodity	Analyte	Fortification level (mg/kg)	n	Range of Recoveries (%)	Mean Recovery (%)	RSD (%)	Method	Reference
Radish Roots	Pyrifluquinazon	0.01	3	90-92	91	1.3	-	R-29108
		0.1	3	106-112	109	2.8		
	quinazolinedione (IV-203)	0.01	3	79–95	87	9.2		
		0.1	3	104-110	108	3.0		
Lettuce	Pyrifluquinazon	0.01	3	82-88	85	3.6	-	
		0.1	3	112-116	114	1.8		
	quinazolinedione (IV-203)	0.01	3	74-103	88	16.5		
		0.1	3	107-112	109	2.3		
Sorghum Forage	Pyrifluquinazon	0.01	3	90-94	92	2.2	-	
		0.1	3	95-100	97	2.6		
	quinazolinedione (IV-203)	0.01	3	82-97	90	8.5		
		0.1	3	105-108	107	1.4		
Sorghum Grain	Pyrifluquinazon	0.01	3	97-107	101	5.2	-	
		0.1	3	89-103	95	7.6		
	quinazolinedione (IV-203)	0.01	3	90-106	100	8.5		
		0.1	3	91-104	98	6.8		

Commodity	Analyte	Fortification level (mg/kg)	n	Range of Recoveries (%)	Mean Recovery (%)	RSD (%)	Method	Reference
Sorghum Stover	Pyrifluquinazon	0.01	3	80-87	83	4.2	-	
		0.1	3	83-88	85	3.1		
	quinazolinedione (IV-203)	0.01	3	80-84	81	2.8		
		0.1	3	85-88	87	1.8		

A number of methods have been reported in the scientific literature for the analysis of pyrifluquinazon and IV-01 in agricultural commodities. You *et al.* (2017) reported a modified LC-MS/MS QUECHERs method for determination of pyrifluquinazon and IV-01 in fruits (strawberry, cherry) and vegetables (cucumber, tomato). The method LOQ was 0.01 mg/kg. In a separate report Do *et al.* (2013) reported an HPLC-UV method for detecting pyrifluquinazon in a range of agricultural commodities with LOQs ranging from 0.02 to 0.05 mg/kg.

Residues in food and feedstuffs of animal origin

Table 45 Overview of methods for the analysis of Pyrifluquinazon, IV-01, IV-03, IV-04, IV-15, IV-203 and IV-208 in animal commodities

<table>
<tr><td></td><td></td><td>Method R-29028</td></tr>
<tr><td rowspan="3">Extraction and clean-up</td><td>Analytes</td><td>IV-04, IV-203 (milk)
IV-01, IV-15, IV-203 (liver)
IV-01, IV-03, IV-15, IV-203 (kidney)
IV-203, IV-208 (muscle, fat)</td></tr>
<tr><td>Matrix</td><td>Milk, muscle, liver, fat, kidney</td></tr>
<tr><td>Extraction</td><td>NOTE: Milk and tissue samples were homogenized in the presence of dry ice.
Milk, muscle, fat:
Milk and muscle samples were extracted with acetonitrile. Fat samples were extracted with acetonitrile and water. All samples were then sonicated and mechanically shaken. The contents of Dispersive SPE Citrate Extraction Tube were added, shaken and centrifuged. An aliquot of the extract was transferred to a Dispersive SPE PSA/ENVI-Carb SPE Clean-up Tube, and centrifuged. The contents were then microfilterfuged and aliquots were taken for sampling, diluting with acetonitrile if necessary.

Liver, Kidney:
Extraction and clean-up (liver and kidney):
Samples were extracted with acetonitrile:water (1:1, v/v), centrifuged to separate the solids, which were re-extracted once with acetonitrile:water (1:1, v/v) and once with acetonitrile. The supernatants were combined. An aliquot of the mixture was concentrated in vacuo to dryness and reconstituted in phosphate buffer. ß-Glucuronidase solution was added and the mixture incubated overnight at 40 °C. Acetonitrile was added to the mixture and the contents of a Dispersive SPE Citrate Extraction Tube were added, shaken and centrifuged. An aliquot of the extract was transferred to a Dispersive SPE PSA/ENVI-Carb SPE Clean-up Tube, centrifuged, the contents filtered and aliquots were taken for sampling, diluting with acetonitrile if necessary.</td></tr>
<tr><td rowspan="6">Chromatography</td><td>Type</td><td>LC</td></tr>
<tr><td>Analytical column</td><td>Phenomenex Kinetex C18 column for chromatographic separation</td></tr>
<tr><td>Dimensions</td><td>100 mm, 4.6 mm id</td></tr>
<tr><td>Particle size</td><td>2.6 µm</td></tr>
<tr><td>Injection volume</td><td>5 µL</td></tr>
<tr><td>Mobile phase</td><td>A 0.1% formic acid in water
B 0.1% formic acid in acetonitrile
<table>
<tr><th>Time (min)</th><th>Flow rate (µL/min)</th><th>%A</th><th>%B</th></tr>
<tr><td>0.00</td><td>900</td><td>80</td><td>20</td></tr>
<tr><td>1.00</td><td>900</td><td>80</td><td>20</td></tr>
<tr><td>13.00</td><td>900</td><td>54</td><td>46</td></tr>
<tr><td>13.01</td><td>900</td><td>0</td><td>100</td></tr>
<tr><td>15.50</td><td>900</td><td>0</td><td>100</td></tr>
</table></td></tr>
</table>

		Method R-29028 16.00 900 80 20 19.00 900 80 20
	Flow rate	
	Instrument	Applied Biosystems MDS/SCIEX API 3000 LC-MS/MS
Detection	Quantitative detection	MS/MS ESI ionization. The following masses were monitored: Pyrifluquinazon; 465.2/423.3, 465.2/92.0 (retention time 12.3 min) IV-15; 437.1/93.4, 437.1/107.1 (retention time 8.3 min) IV-01; 423.1/107.1, 423.1/92.2 (retention time 9.4 min) IV-03; 437.08/314.9, 437.08/275.0 (retention time 10.8 min) IV-04; 435.05/279.9, 435.05/274.8 (retention time 11.2 min) IV-208; 371.96/99.0, 371.96/262.0 (retention time 11.3 min) IV-203; 329.1/309.4, 329.1/239.8, 329.1/222.9, 329.1/288.8 (retention time 11.6 min)
	LOQ	0.005 mg/kg (milk) 0.01 mg/kg (liver, kidney, muscle, fat)
	Whole method linearity (r^2)	0.5-1.0 ng/mL r≥0.99

Recovery and repeatability data for the determination of IV-01, IV-03, IV-04, IV-15, IV-203 and IV-208 residues in animal commodities are presented in Table 46 (Mannella 2016 A-29022). Average recoveries ranged from 72 to 117%. The LOQ was 0.005 mg/kg for milk and 0.01 mg/kg for tissues. The %RSDs ranged from 2–18.

Calibration curves over the range 0.5–1.0 ng/mL for each analyte demonstrated linearity with $r \geq 0.99$.

Table 46 Recovery data for metabolites of pyrifluquinazon in animal commodities (R-29022)

Commodity	Analyte	Fortification level (mg/kg)	n	Range of Recoveries (%)	Mean Recovery (%)	RSD (%)	Method	Reference
Milk	IV-04	0.005	5	88-105	95	7	-	A-29028
		0.05	5	95-110	101	6		
	IV-203	0.005	5	70-81	76	7		
		0.05	5	82-94	89	6		
Liver [a]	IV-01	0.01	8	53-100	77	21	-	
		0.1	8	40-85	68	26		
	IV-15	0.01	8	62-112	95	16		
		0.1	8	64-105	92	14		
	IV-203	0.01	8	58-119	97	21		
		0.1	8	59-113	90	17		
Kidney	IV-01	0.01	5	61-88	78	15	-	
		0.1	5	89–98	93	4		
	IV-03	0.01	5	50-84	72	18		
		0.1	5	81-87	84	2		
	IV-15	0.01	5	71-99	89	12		
		0.1	5	98-109	104	6		
	IV-203	0.01	5	63-96	84	14		
		0.1	5	99-124	108	8		
Muscle	IV-203	0.01	5	75-89	83	7	-	
		0.1	5	103-109	106	3		
	IV-208	0.01	5	100-119	110	7		
		0.1	5	104-120	112	6		

Commodity	Analyte	Fortification level (mg/kg)	n	Range of Recoveries (%)	Mean Recovery (%)	RSD (%)	Method	Reference
Fat	IV-203	0.01	5	79–91	83	6	-	
		0.1	5	103-113	109	4		
	IV-208	0.01	5	86-118	99	12		
		0.1	5	113-119	117	3		

[a] Combined recoveries are reported from enzyme digest on total and portion of extract. If values identified as outliers are excluded recoveries were for IV-01 0.01 mg/kg, n = 6 range 73-100%, mean 85%, %RSD 11, 0.1 mg/kg, n = 6, range 65-85%, mean 77%, %RSD 11; IV-15 0.01 mg/kg n = 7 range 87-112%, mean 100%, %RSD 9, 0.1 mg/kg n = 7 range 89-105%, mean 96%, %RSD 6; IV-203 0.01 mg/kg n = 7 range 74-119, mean 102%, %RSD 14, 0.1 mg/kg n = 7 range = 87-113, mean 94%, %RSD 9.

Multi-residue method

Pyrifluquinazon and metabolites IV-01, IV-02, IV-15, IV-27, IV-28, and IV-203 have been tested using the Food and Drug Administration (FDA) multi-residue method (MRM) protocols. Testing results indicate that these methods are not suitable for determination of pyrifluquinazon or any of the metabolites.

Extraction efficiency

The results of the plant metabolism studies of pyrifluquinazon showed that residues are substantially extracted when acetonitrile or acetonitrile:0.1 N HCl (4:1, v/v) is used as the extraction solvent.

Marin (2012 A-29022) studied the extraction efficiency of the residue analytical methods in livestock.

Samples of milk, liver, kidney, muscle and fat containing incurred Qn-^{14}C residues from the goat metabolism study (R-29058) were extracted in accordance with method R-29028 and in accordance with the method extraction used in the metabolism study.

In order to demonstrate storage stability of pyrifluquinazon metabolites in the stored metabolism study samples, the samples were re-extracted using the metabolism method extraction and analysed by HPLC. These results were compared with the original results obtained in 2008 (R-29058).

Note tissue samples in the metabolism study were cryogenically homogenised and stored frozen prior to analysis. Initial extractions took place 20 to 34 days after sacrifice for tissues and 85 days in the case of milk fat. HPLC and TLC analysis took place 22 (liver) to 108 (subcutaneous fat, renal fat, milk fat) days after sacrifice.

The TRR results determined in 2011 and 2008 are summarized in Table 47. The percent relative recovery of the non-exhaustive extractions was ≥ 88%. No whole milk TRR data were determined in 2008, where analysis of the skim milk and milk fat were conducted. However, the percent mass of skim milk and milk fat, as well as the respective TRRs, were used to calculate a TRR in whole milk.

The radio-chromatogram profiles, and where conducted 2D-TLC plates, of samples were in general comparable to those obtained from the original 2008 samples. The radio-chromatogram results are summarized in Table 48. Pyrifluquinazon metabolites appear stable under freezer conditions in animal tissues and milk for over 3 years.

Table 47 Comparison of TRR and extraction efficiencies of Qn-label experiment

Matrix	TRR in 2011	TRR in 2008	Recovery [a]
Milk (4-day, PM)	0.798	0.812	98.3
Liver	3.158	3.500	90.2

Matrix	TRR in 2011	TRR in 2008	Recovery [a]
Kidney	0.627	0.685	91.5
Loin muscle	0.103	0.115	89.6
Renal fat	0.175	0.198	88.4

[a] Percent recovery of the 2008 values

Table 48 Comparison of metabolite residues in samples from Qn-label experiment

Matrix	Metabolite	Concentration in 2011 (mg/kg)	Concentration in 2008 (mg/kg)
Whole milk	IV-04	0.599	0.641[c]
	IV-203	0.108	0.081[c]
Liver	IV-01+IV-15	2.447 [a]	2.517 [a]
	IV-203	0.426	0.438
Kidney	IV-01+IV-15	0.213 [a]	0.240 [a]
	IV-03	0.060	0.081
	IV-203	0.222	0.250
Muscle	IV-203	0.058	0.075
	IV-208	0.014	0.017
Fat	IV-203	0.135 [b]	0.119
	IV-208		0.013

[a] Sum of IV-01, IV-15 and glucuronide conjugates that co-chromatographed.

[b] IV-203 and IV-208 co-eluted

[c] whole milk values reconstructed from slimmed milk and milk fat results using a milk fat content for whole milk of 7.5%

The validated residue method was used to determine the residues of metabolites in the tissues from the Qn-label goat metabolism study. Procedural recoveries were also conducted alongside the analysis, demonstrating acceptable performance of the method (70–120%). Procedural recoveries are summarized in Table 49. Residues determined by the residue method were compared to those established by the current metabolism method results (Table 50). The residue method shows good agreement with the metabolism method.

Table 49 Summary of procedural recovery data for animal commodities

Commodity	Analyte	Fortification level (mg/kg)	n	Range of Recoveries (%)	Mean Recovery (%)	Reference
Milk	IV-04	0.005	1	98	-	A-29022
		0.05	1	96	-	
	IV-203	0.005	1	79	-	
		0.05	1	89	-	
Liver†	IV-01	0.01	3	73-83	78	
		0.1	3	75-85	81	
	IV-15	0.01	3	87-103	96	
		0.1	3	89–93	91	
	IV-203	0.01	3	74-119	101	
		0.1	3	87-93	90	
Kidney	IV-01	0.01	3	87-96	92	
		0.1	3	88	88	
	IV-03	0.01	3	82-92	89	
		0.1	3	70-86	77	
	IV-15	0.01	3	112-118	116	
		0.1	3	96-102	99	
	IV-203	0.01	3	86-110	95	
		0.1	3	95-98	96	

Commodity	Analyte	Fortification level (mg/kg)	n	Range of Recoveries (%)	Mean Recovery (%)	Reference
Muscle	IV-203	0.01	1	97	-	
		0.1	1	97	-	
	IV-208	0.01	1	112	-	
		0.1	1	107	-	
Fat	IV-203	0.01	1	88	-	
		0.1	1	82	-	
	IV-208	0.01	1	100	-	
		0.1	1	107	-	

Table 50 Radiovalidation: comparison of metabolism and residue analysis methods

Matrix	Metabolite	Concentration by metabolism method (mg/kg)	Mean concentration by residue analytical method (mg/kg)
Milk	IV-04	0.599	0.541
	IV-203	0.108	0.046
Liver	IV-01	1.284 [a]	1.293
	IV-15	0.192 [a]	0.234
	IV-203	0.706	0.513
Kidney	IV-01	0.103 [a]	0.100
	IV-15	0.010 [a]	0.015
	IV-03	ND	< 0.01
	IV-203	0.250	0.234
Muscle	IV-203	0.058	0.074
	IV-208	0.014	0.000
Fat	IV-203	0.135 [b]	0.093
	IV-208	-	0.000

[a] As determined by 2D TLC after enzyme digestion.

[b] IV-203 and IV-208 co-elute

The residues of pyrifluquinazon metabolites in Qn-label milk and tissues are stable under freezer conditions over a period of approximately 3 years. The residue analytical method described in A-29022 accurately reflects the residues of pyrifluquinazon metabolites determined in the metabolism study, demonstrating that the residue analytical method efficiently extracts pyrifluquinazon metabolites from milk and animal tissues.

Stability of pesticide residues in stored analytical samples

A number of studies of the stability pyrifluquinazon and IV-01 in plant commodities and pyrifluquinazon following freezer storage of samples were made available to the Meeting.

Brown (2012 R-29043) investigated the deep freeze stability of pyrifluquinazon and 1H (IV-01) in almond nutmeats, apples, cauliflower, cottonseed, cotton gin by-products, cottonseed hulls, cottonseed refined oil, cucumbers, grapes, head lettuce, oranges, orange dried pulp, orange juice, peaches, potatoes, tomatoes and tomato paste over a period of 18 months. Except for oils, homogenised frozen control samples were separately fortified with 0.1 mg/kg of pyrifluquinazon or 1H (IV-01) and stored deep frozen at -20 ± 5 °C (except for the day 0 samples). Processed oil samples were weighed out semi-frozen, fortified and kept in semi-frozen state until extraction.

Fortified stability samples and control samples were prepared for analysis at intervals ranging from 0-day to 18 months. Each analysis set (except 0 day) consisted of one procedural control, two procedural fortifications and two stability fortifications. Zero day analysis sets consisted of one control sample and two procedural fortifications.

Residue analysis was performed according to Analytical Method #Meth-188, rev. 2 and 3.

For several matrices, it was necessary to restart the stability evaluations in order to improve recoveries, include shorter storage intervals and analyse missed storage intervals. These restarts were implemented for cauliflower, cotton gin by-products, cucumbers, head lettuce and tomatoes.

In the original storage stability evaluations for cotton gin by-products, head lettuce and tomatoes Revision #2 of the analytical method was used where the samples were weighed and fortified in a totally thawed state. For the original stability evaluations of cauliflower and cucumbers and restarts of all matrices the samples were weighed and fortified in a frozen state following Revision #3 of the analytical method, which minimised degradation of analytes prior to freezing.

The uncorrected recoveries from the stored fortified and the concurrent recoveries from the freshly fortified samples are presented in Table 51 for pyrifluquinazon and 1H (IV-01).

The mean concurrent recoveries across all matrices and storage intervals were in the range of 83–118% for pyrifluquinazon and 81–124% for 1H (IV-01). In assessing the stability studies it was noted that contradictory results were sometimes obtained. In such cases stability was judged as the period where all studies agreed. Pyrifluquinazon and 1H (IV-01) were considered stable in high oil commodities nutmeat and cottonseed for at least 163 and 366 days, respectively. Pyrifluquinazon and 1H (IV-01) were considered stable in high acid commodities grape and orange for at least 194 and 158 days, respectively. Pyrifluquinazon was considered stable in high starch commodity potato for at least 365 days, and 1H (IV-01) was considered stable in high starch commodity potato for at least 183 days (based on corrected mean recovery of 68% being sufficiently close to 70% to demonstrate stability).

Storage stability in high water commodities was variable (Table 51). Pyrifluquinazon was stable in apples for 157 days, cucumber for 66 days, grape for 194 days, lettuce for 93 days, peach for 377 days and tomato for 93 days. 1H (IV-01) in apples, cucumber, grape, lettuce, peach, tomato ranged from unstable (tomato), to stable for 31 days (cucumber) to stable for at least 377 days (peach). Cauliflower demonstrated particularly low recoveries for 1H (IV-01), and was not stable in this matrix. Acceptable stability of pyrifluquinazon in cauliflower was observed for 102 days.

Storage stability of pyrifluquinazon in processed commodities also varied from 182 days for cottonseed refined oil to 546 days for tomato paste. Storage stability of 1H (IV-01) in processed commodities varied from 106 days for cottonseed refined oil to 546 days for tomato paste.

Table 51 Stability of pyrifluquinazon and 1H (IV-01) residues fortified at 0.1 mg/kg in crops following storage at -20 °C ± 5 °C

Commodity	Storage interval (days)		Pyrifluquinazon			1H (IV-01)		
			Residue (mg/kg)	Mean % remaining	Procedural recovery (mean, %)	Residue (mg/kg)	Mean % remaining	Procedural recovery (mean, %)
Almond Nutmeats	0	Original	-	100.0	102	-	100.0	98
	63	Original	0.103, 0.0998	101.4	108	0.110, 0.0972	103.6	108
	163	Original	0.102, 0.103	102.5	103	0.105, 0.106	105.5	102
Apples	0	Original	-	100.0	100	-	100.0	102
	66	Original	0.0832, 0.0862	84.7	103	0.0860, 0.0912	88.6	119
	157	Original	0.0740, 0.0800	77.0	92	0.0768, 0.0802	78.5	92
Cauliflower	0	Original	-	100.0	100	-	100.0	101
	66	Original	0.0692, 0.0642	66.7	108	0.0180, 0.0252	21.6	118
	0	Restart 1	-	100.0	94	-	100.0	90
	249	Restart 1	0.0428, 0.0492	46.0	97	0.0385, 0.0360	37.3	98
	0	Restart 2	-	100.0	92	-	100.0	99
	41	Restart 2	0.0508, 0.0590	54.9	91	0.0178, 0.00882	13.3	94

Commodity	Storage interval (days)		Pyrifluquinazon			1H (IV-01)		
			Residue (mg/kg)	Mean % remaining	Procedural recovery (mean, %)	Residue (mg/kg)	Mean % remaining	Procedural recovery (mean, %)
	80	Restart 2	0.0495, 0.0622	55.9	94	0.0103, 0.0120	11.2	98
	0	Restart 3	-	100.0	92	-	100.0	98
	7	Restart 3	0.0828, 0.0838	83.3	92	0.0558, 0.0650	60.4	104
	14	Restart 3	0.0808, 0.0768	78.8	91	0.0568, 0.0500	53.4	107
	21	Restart 3	0.0832, 0.0782	80.7	100	0.0532, 0.0722	62.7	113
	31	Restart 3	0.0825, 0.0805	81.5	96	0.0578, 0.0550	56.4	98
	70	Restart 3	0.0815, 0.0738	77.7	103	0.0435, 0.0525	48.0	107
	102	Restart 3	0.0788, 0.0648	71.8	101	0.0240, 0.0355	29.8	103
Cottonseed	0	Original	-	100.0	101	-	100.0	106
	30	Original	0.0730, 0.0752	74.1	100	0.0770, 0.0772	77.1	98
	93	Original	0.0630, 0.0712	67.1	98	0.0905, 0.0867	88.6	98
	182	Original	0.0660, 0.0648	65.4	96	0.730, 0.0592	66.1	96
	366	Original	0.0820, 0.0632	72.6	100	0.0805, 0.0692	74.9	96
Cotton Gin Byproducts	0	Original	-	100.0	102	-	100.0	104
	35	Original	0.0408, 0.0448	42.8	103	0.0562, 0.0542	55.2	98
	94	Original	0.0330, 0.0368	34.9	94	0.0458, 0.0345	40.2	92
	182	Original	0.0250, 0.0312	28.1	100	0.0570, 0.0402	48.6	101
	368	Original	0.0201, 0.0157	17.9	92	0.0485, 0.0310	39.8	94
	0	Restart 1	-	100.0	97	-	100.0	99
	14	Restart 1	0.0842, 0.0918	88.0	90	0.0838, 0.0865	85.2	82
	64	Restart 1	0.0830, 0.0778	80.4	98	0.0850, 0.0835	84.3	100
	393	Restart 1	0.0725, 0.0675	70.0	88	0.0652, 0.0702	67.7	83
Cottonseed Hulls	0	Original	-	100.0	94	-	100.0	95
	30	Original	0.0745, 0.0702	72.4	91	0.0695, 0.0708	70.2	88
	93	Original	0.0640, 0.0695	66.8	83	0.0636, 0.0628	63.2	81
	181	Original	0.0710, 0.0690	70.0	90	0.0665, 0.0600	63.3	88
	365	Original	0.0628, 0.0642	63.5	90	0.0605, 0.0585	59.5	86
Cottonseed Refined Oil	0	Original	-	100.0	91	-	100.0	103
	35	Original	0.0812, 0.0820	81.6	88	0.0802, 0.0858	83.0	92
	106	Original	0.0858, 0.0860	85.9	94	0.0812, 0.0800	80.6	93
	182	Original	0.0775, 0.0748	76.2	91	0.0538, 0.0642	59.0	98
	365	Original	0.0678, 0.0698	68.8	86	0.0370, 0.0358	36.4	82

Commodity	Storage interval (days)		Pyrifluquinazon			1H (IV-01)		
			Residue (mg/kg)	Mean % remaining	Procedural recovery (mean, %)	Residue (mg/kg)	Mean % remaining	Procedural recovery (mean, %)
Cucumbers	0	Original	-	100.0	98	-	100.0	101
	66	Original	0.0725, 0.0770	74.8	108	0.0522, 0.0478	50.0	114
	0	Restart 1	-	100.0	94	-	100.0	103
	262	Restart 1	0.0588, 0.0410	49.9	96	0.0187, 0.0260	22.4	100
	0	Restart 2	-	100.0	102	-	100.0	98
	31	Restart 2	0.0718, 0.0800	75.9	98	0.0840, 0.0745	79.3	98
	62	Restart 2	0.0628, 0.0682	65.5	92	0.0555, 0.0570	56.3	96
	90	Restart 2	0.0665, 0.0608	63.7	86	0.0460, 0.0402	43.1	88
Grapes	0	Original	-	100.0	101	-	100.0	102
	63	Original	0.0872, 0.0895	88.4	118	0.100, 0.0998	99.9	124
	194	Original	0.0960, 0.0795	87.8	96	0.0792, 0.0898	84.5	92
Head Lettuce	0	Original	-	100.0	99	-	100.0	100
	35	Original	0.0790, 0.0835	81.3	106	0.0808, 0.0928	86.8	105
	94	Original	0.0540, 0.0600	57.0	88	0.0543, 0.0623	58.3	90
	182	Original	0.0520, 0.0535	52.8	96	0.0465, 0.0448	45.7	100
	0	Restart 1	-	100.0	99	-	100.0	98
	31	Restart 1	0.0875, 0.0850	86.3	97	0.0718, 0.0728	72.3	99
	90	Restart 1	0.0690, 0.0698	69.4	104	0.0580, 0.0615	59.8	102
	186	Restart 1	0.0565, 0.0500	53.3	88	0.0478, 0.0420	44.9	92
	0	Restart 2	-	100.0	92	-	100.0	91
	30	Restart 2	0.0722, 0.0842	78.2	92	0.0685, 0.0685	68.5	98
	61	Restart 2	0.0752, 0.0700	72.6	90	0.0730, 0.0685	70.8	90
	93	Restart 2	0.0760, 0.0710	73.5	100	0.0412, 0.0482	44.7	101
	170	Restart 2	0.0600, 0.0450	52.5	86	0.0608, 0.0622	61.5	97
Oranges	0	Original	-	100.0	92	-	100.0	90
	64	Original	0.102, 0.0880	95.0	111	0.0980, 0.0940	96.0	120
	158	Original	0.0920, 0.0932	92.6	96	0.0918, 0.0840	87.9	95
Orange Dried Pulp	0	Original	-	100.0	106	-	100.0	104
	35	Original	0.0982, 0.0975	97.9	107	0.0805, 0.0865	83.5	99
	95	Original	0.0792, 0.0758	77.5	100	0.0735, 0.0798	76.7	102
	184	Original	0.0760, 0.0762	76.1	103	0.0735, 0.0870	80.3	110
	367	Original	0.0732, 0.0768	75.0	100	0.0558, 0.0658	60.8	100
Orange	0	Original	-	100.0	99	-	100.0	100

Commodity	Storage interval (days)		Pyrifluquinazon			1H (IV-01)		
			Residue (mg/kg)	Mean % remaining	Procedural recovery (mean, %)	Residue (mg/kg)	Mean % remaining	Procedural recovery (mean, %)
Juice								
	31	Original	0.0985, 0.0982	98.4	98	0.0988, 0.0950	96.9	102
	94	Original	0.0942, 0.0890	91.6	95	0.0975, 0.0980	97.8	96
	181	Original	0.0920, 0.0928	92.4	98	0.0895, 0.0905	90.0	99
	365	Original	0.0805, 0.0842	82.4	97	0.0750, 0.0795	77.3	91
Peaches	0	Original	-	100.0	92	-	100.0	90
	64	Original	0.0942, 0.0988	96.5	114	0.106, 0.101	103.5	120
	377	Original	0.0938, 0.0992	96.5	112	0.0915, 0.0950	93.3	118
Potatoes	0	Original	-	100.0	93	-	100.0	98
	33	Original	0.0778, 0.0805	79.2	90	0.0655, 0.0615	63.5	93
	93	Original	0.0712, 0.0778	74.5	86	0.0720, 0.0655	68.8	84
	183	Original	0.0618, 0.0752	68.5	94	0.0623, 0.0716	67.0	98
	365	Original	0.0642, 0.0735	68.9	89	0.0592, 0.0500	54.6	90
Tomatoes	0	Original	-	100.0	104	-	100.0	104
	30	Original	0.0790, 0.0750	77.0	100	0.0755, 0.0825	79.0	98
	93	Original	0.0605, 0.0810	70.8	102	0.0785, 0.0662	72.4	105
	181	Original	0.0502, 0.0528	51.5	97	0.0518, 0.0575	54.7	101
	0	Restart 1	-	100.0	106	-	100.0	110
	31	Restart 1	0.0818, 0.0725	77.2	99	0.0610, 0.0652	63.1	96
	91	Restart 1	0.0632, 0.0572	60.2	102	0.0570, 0.0460	51.5	108
	184	Restart 1	0.0320, 0.0305	31.3	98	0.0348, 0.0315	33.2	94
	260	Restart 1	0.0398, 0.0378	38.8	112	0.0450, 0.0422	43.6	120
	0	Restart 2	-	100.0	102	-	100.0	105
	30	Restart 2	0.0575, 0.0665	62.0	89	0.0612, 0.0538	57.5	95
	61	Restart 2	0.0668, 0.0750	70.9	88	0.0485, 0.0528	50.7	86
	93	Restart 2	0.0682, 0.0500	59.1	102	0.0412, 0.0405	40.9	104
	170	Restart 2	0.0670, 0.0420	54.5	86	0.0598, 0.0598	59.8	99
	223	Restart 2	0.0738, 0.0452	59.5	100	0.0628, 0.0605	61.7	102
Tomato Paste	0	Original	-	100.0	95	-	100.0	100
	32	Original	0.0975, 0.0972	97.4	98	0.0912, 0.0872	89.2	92
	94	Original	0.0822, 0.0808	81.5	92	0.0920, 0.0865	89.3	91
	195	Original	0.0868, 0.0880	87.4	96	0.0985, 0.0952	96.9	94
	368	Original	0.0792,	76.7	86	0.0710,	73.4	87

Commodity	Storage interval (days)		Pyrifluquinazon			1H (IV-01)		
			Residue (mg/kg)	Mean % remaining	Procedural recovery (mean, %)	Residue (mg/kg)	Mean % remaining	Procedural recovery (mean, %)
			0.0742			0.0758		
	546	Original	0.0692, 0.0698	69.5	88	0.0730, 0.0728	72.9	86

Recoveries are reported as uncorrected

As part of the rotational crop field accumulation study, the stability of parent pyrifluquinazon and its metabolite IV-203 was investigated in radish, lettuce and sorghum matrices upon frozen storage at -20 ± 5 °C. All fortifications were conducted at 0.1 mg/kg for all matrices. Fortification was performed using a mixed standard solution prepared in acetonitrile. Unfortified samples were stored under the same conditions to serve as control material for concurrent recovery determination.

Residue analysis was performed according to the analytical method validated in R-29108.

Restarts were conducted for lettuce, sorghum forage and stover due to the original periods tested being too long to demonstrate stability of IV-203.

The uncorrected recoveries from the stored fortified and the concurrent recoveries from the freshly fortified samples are presented in Table 52 for pyrifluquinazon and IV-203.

Table 52 Stability of pyrifluquinazon and IV-203 residues in crops following storage at -20 °C ± 5 °C

Commodity	Storage interval (days)	Initiation status	pyrifluquinazon			IV-203		
			Residue (mg/kg)	Mean %remaining	Procedural recovery (mean, %)	Residue (mg/kg)	Mean % remaining	Procedural recovery (mean, %)
Radish	0	Original	-	100.0	109	-	100.0	108
Roots	67	Original	0.0842, 0.0820	83.1	101	0.0710, 0.0732	72.1	105
Lettuce	0	Original	-	100.0	114	-	100.0	109
	169	Original	0.0535, 0.0552	54.4	88	0.0585, 0.0555	57.0	90
	0	Restart	-	100.0	101	-	100.0	99
	81	Restart	0.0775, 0.0728	75.2	103	0.106, 0.101	103.5	99
Sorghum Forage	0	Original	-	100.0	97	-	100.0	107
	168	Original	0.0668, 0.0702	68.5	87	0.0622, 0.0592	60.7	90
	0	Restart	-	100.0	97	-	100.0	98
	129	Restart	-		-	0.105, 0.102	103.5	93
Sorghum Grain	0	Original	-	100.0	95	-	100.0	98
	93	Original	0.0822, 0.0808	81.5	86	0.0912, 0.0890	90.1	85
Sorghum Stover	0	Original	-	100.0	85	-	100.0	87
	165	Original	0.0758, 0.0750	75.4	80	0.0472, 0.0470	47.1	79
	0	Restart	-	100.0	-	-	100.0	102
	77	Restart	-		-	0.109, 0.106	107.5	102

The stability of pyrifluquinazon, 1H (IV-01) and IV-203 residues in high water, high oil, high starch, high acid and processed commodities when stored at -20 ± 5 °C is summarized in Table 53.

Table 53 Summary of demonstrated stability on frozen storage

Matrix	Pyrifluquinazon	1H (IV-01)	IV-203
Almond nutmeat	163	163	
Apple	157	157	
Cauliflower	31	Not stable	
Cottonseed	366	366	
Cotton gin by-products	393	64	
Cottonseed hulls	181	30	
Cottonseed refined oil	182	106	
Cucumber	66	31	
Grapes	194	194	
Head lettuce	61	61	81
Orange	158	158	
Orange dried pulp	367	184	
Orange juice	365	365	
Peaches	377	377	
Potato	93	Not stable	
Radish roots	67		67
Sorghum forage	168		129
Sorghum grain	93		93
Sorghum stover	165		77
Tomato	61	Not stable	
Tomato paste	546	546	

Pyrifluquinazon is stable in a range of high water commodities (apple 157, cauliflower 31, cucumber 66, lettuce 61, peaches 377 and tomatoes 61 days), high oil (almonds 163, cottonseed 366), high acid (grapes 194, oranges 158) and high starch (potato 93, radish 67, sorghum 93) though the stability interval varied widely between crops. Metabolite 1H (IV-01) had similar or lower stability than pyrifluquinazon and is stable in high water commodities (apple 157 days, cauliflower not stable, cucumber 31 days, lettuce 61 days, peaches 377 days and tomatoes not stable), high oil (almonds 163 days, cottonseed 366 days), high acid (grapes 194 days, oranges 158 days) and high starch (potato not stable).

The demonstrated stability intervals on frozen storage encompass the duration of storage in the residue trials evaluated by the Meeting.

USE PATTERNS

Pyrifluquinazon is to a quinazinalone insecticide for the control of control of sap-feeding insects, including whiteflies, aphids, leafhoppers, thrips, and mealybugs. It acts by modification of insect feeding behaviour.

Pyrifluquinazon is intended for use as an insecticide on plum, potato, tree nuts and tea.

Pyrifluquinazon is registered for use in tea in Japan and a range of crops including plum, potato and tree nuts in the USA.

Table 54 Use patterns

Crop	Country	Form	Application				PHI days	Comment
			Rate, g ai/ha	Spray volume L/ha	Spray conc. g ai/hL	No.(interval)		
Stone fruit	USA	SC	39 – 53, max/year 78	935	4-6	2 (min 7 days between applications)	7	
Tuberous and Corm vegetables	USA	SC	39 – 53, max/year Florida 78, max/year other states 105	187 or if using chemigation a minimum of 0.25–0.64 ha-cm of water	21-28	2 (min 14 days between applications)	14	Do not feed tops to livestock
Tree nuts	USA	SC	39-53, max/year 78	935	4-6	2 (min 7 days between applications)	7	
Tea	Japan	WG		2000-10,000	6.7-10	2	7	

Stone Fruits (Crop Group 12-12) [Not for use in California]: apricot; apricot, Japanese; capulin; cherry, black; cherry, Nanking; cherry, sweet; cherry, tart; Jujube, Chinese; nectarine; peach; plum; plum, American; plum, beach; plum, Canada; plum, cherry; plum, Chickasaw; plum, Damson; plum, Japanese; plum, Klamath; plum, prune; plumcot; sloe; cultivars, varieties, and/or hybrids of these

Tree Nuts (Crop Group 14-12) [Not for use in California] African nut-tree; almond; beechnut; Brazil nut; Brazilian pine; bunya; bur oak; butternut; Cajou nut; candlenut; cashew; chestnut; chinquapin; coconut; coquito nut; dika nut; ginkgo; Guiana chestnut; hazelnut (filbert); heartnut; hickory nut; Japanese horsechestnut; macadamia nut; mongongo nut; monkey-pot; monkey puzzle nut; Okari nut; Pachira nut; peach palm nut; pecan; pequi; Pili nut; pine nut; pistachio; Sapucaia nut; tropical almond; walnut, black; walnut, English; yellowhorn; cultivars, varieties, and/or hybrids of these

Tuberous and Corm Vegetables (Crop Subgroup 1C) [Not for use in California] Arracacha; arrowroot; artichoke, Chinese; artichoke, Jerusalem; canna, edible; cassava, bitter and sweet; chayote (root); chufa; dasheen (taro); ginger; leren; potato; sweet potato; tanier; turmeric; yam bean; yam, true

For maximum performance, the use instructions recommend the use of an agricultural spray adjuvant with pyrifluquinazon.

The US label also contains rotational crop restrictions. For crops on the label there is no restriction. For Herbs (US EPA crop subgroup 19A) and stalk and stem vegetables (US EPA Crop Subgroup 22A) the PBI is 60 days and for all other crops it is 365 days.

RESULTS OF SUPERVISED RESIDUE TRIALS ON CROPS

The Meeting received information on supervised field trials for pyrifluquinazon on the following crops or crop groups:

Crop	Table No.
Stone fruit (cherries, peaches, plums)	55-57
Root & tuber vegetables (potato)	58
Tree nuts	59-60
Tea	61
Almond hulls	62

Trials were generally well documented, with laboratory and field reports. Laboratory reports included method validation with procedural recoveries from spiking at residue levels similar to those occurring in samples from the supervised trials. Dates of analyses or duration of residue sample storage were also provided. Although trials included control plots, no control data are recorded in the tables except where residues in control samples exceeded the LOQ. Control samples are indicated in

the summary tables with a "c". Unless stated otherwise, residue data are recorded unadjusted for recovery.

Residues and application rates have generally been rounded to two significant figures or, for residues near the LOQ, to one significant figure. Residue values from the trials conducted according to maximum GAP have been used for the estimation of maximum residue levels. Those results included in the evaluation are underlined.

Conditions of the supervised residue trials were generally well reported in detailed field reports. Trial designs used non-replicated plots. Field reports provided data on the sprayers used, plot size, field sample size and sampling date.

Stone fruit

Wyatt (2011 R-29115) conducted twenty-one residue trials on stone fruit (6 cherry, 6 plum, 9 peach) in the USA in 2010. In each trial pyrifluquinazon was applied three times with an interval of 7 days as a foliar spray of an SC formulation at a nominal rate of 50 g ai/ha with a PHI of 7 days. In one plum trial a separate plot was treated at 5× the normal rate (3 × 250 g ai/ha) in order to provide samples of fruit for a processing study. All applications included a non-ionic surfactant. The samples obtained at harvest were frozen for a maximum of 83 days before extraction and analysis. Fruit was analysed for residues of pyrifluquinazon and metabolite 1H (IV-01) using the analytical method No. Meth-188, rev. 3, with an LOQ of 0.01 mg/kg and LOD of 0.003 mg/kg for each analyte. Acceptable concurrent recovery data were obtained for all matrices. Concurrent recoveries of pyrifluquinazon and 1H (IV-01) in tart cherry fruit ranged from 79-89% (mean = 85 ± 4.3%, n = 4) and 83-91% (mean = 86 ± 3.3%, n = 5), respectively. Concurrent recoveries of pyrifluquinazon and 1H (IV-01) in sweet cherry fruit ranged from 79–96% (mean = 90 ± 7.4%, n = 4) and 88-101% (mean = 93 ± 5.7%, n = 4), respectively. Concurrent recoveries of pyrifluquinazon and 1H (IV-01) in peach fruit ranged from 82-108% (mean = 93 ± 7.6%, n = 10) and 86-109% (mean = 96 ± 7.8%, n = 10), respectively. Concurrent recoveries of pyrifluquinazon and 1H (IV-01) in plum fruit ranged from 78-104% (mean = 95 ± 7.9%, n = 10) and 72-120% (mean = 98 ± 12%, n = 10), respectively. Concurrent recoveries of pyrifluquinazon and 1H (IV-01) in prunes ranged from 92-96% (mean = 94%, n = 2) and 94-99% (mean = 96%, n = 2), respectively.

The pitted samples were ground to a homogeneous consistency in the presence of dry ice. The ground samples and subsamples were placed in frozen storage immediately after grinding and subsampling. For all ground samples in this study, the dry ice was allowed to sublime prior to weighing the samples for extraction. Samples were extracted within 1 to 20 days of grinding.

Table 55 Residues of pyrifluquinazon in cherries (Wyatt 2011 R-29115) (duplicate field samples, i.e. two samples per plot) [a]

Location, year, variety CHERRY	N (int)	Rate g ai/ha	Vol L/ha	GS application	DALA	Sample	Residues (mg/kg) Pyrifluquinazon	1H (IV-01)[b]	Sum
Alton NY, USA 2010 Montmorency [c]	3 (7 7)	52	571	BBCH 79	7	Fruit	< 0.01 < 0.01	0.0864	0.097
		50	561	BBCH 81				0.0830	0.094
		52	571	BBCH 85					
	3 (7 7)	50	1132	BBCH 79	7	Fruit	< 0.01 < 0.01	0.127 0.106	0.138
		49	1122	BBCH 81					0.117
		49	1113	BBCH 85					
Conklin MI USA 2010 Montmorency	3 (7 7)	50	1908	BBCH 75	7	Fruit	< 0.01 < 0.01	0.0957	0.1065
		50	1880	BBCH 81				0.0993	0.11
		50	1889	BBCH 85					
Marengo IL USA 2010 North Star	3 (7 7)	46	664	BBCH 81	7	Fruit	< 0.01 < 0.01	0.0641	0.0756
		45	636	BBCH 83				0.0588	0.0704

Location, year, variety CHERRY	N (int)	Rate g ai/ha	Vol L/ha	GS application	DALA	Sample	Residues (mg/kg) Pyrifluquinazon	1H (IV-01)[b]	Sum
		45	617	BBCH 85					
Plainview CA USA 2010 Tulare [D]	3(6 7)	45	543	BBCH 75	7	Fruit	< 0.01 < 0.01	0.0182	0.0365
		45	552	BBCH 77				0.0138	0.0297
		45	524	BBCH 79					
	3 (6 7)	45	2759	BBCH 75	0	Fruit	0.0612 0.0508	0.0710	0.142
		45	2712	BBCH 77				0.0588	0.120
		45	2825	BBCH 79					
					7	Fruit	< 0.01 < 0.01	0.0131	0.0239
								0.0126	0.0234
					14	Fruit	< 0.01 < 0.01	< 0.01	< 0.02
								< 0.01	< 0.02
					21	Fruit	< 0.01 < 0.01	< 0.01	< 0.02
								< 0.01	< 0.02
Ephrata WA USA 2010 Bing	3 (7 7)	50	2376	BBCH 81	7	Fruit	< 0.01 < 0.01	0.0203	0.0346
		50	2366	BBCH 85				0.0199	0.0341
		50	2376	BBCH 87					
Weiser ID USA 2010 Kiona	3 (8 7)	49	561	BBCH 77	7	Fruit	< 0.01 < 0.01	0.0205	0.0380
		50	561	BBCH 81				0.0167	0.0325
		50	571	BBCH 84					

[a] All applications included a non-ionic surfactant

[b] Residues of 1H (IV-01) are expressed as pyrifluquinazon equivalents

[c] trials at Alton NY USA 2010 are not independent, the spray dates were the same for both trials, 22/6, 29/6 and 6/7

[d] trials at Plainview CA USA 2010 are not independent, the spray dates were the same for both trials, 13/4, 19/4, 26/4

Table 56 Residues of pyrifluquinazon in peach (Wyatt 2011 R-29115)[a]

Location, year, variety PEACH	N (int)	Rate g ai/ha	Vol L/ha	GS application	DALA	Sample	Residues (mg/kg) Pyrifluquinazon	1H (IV-01)[b]	Sum
Alton NY, USA 2010 Red Haven [c]	3 (7 7)	50	561	BBCH 75	7	Fruit	< 0.01 < 0.01	< 0.01	< 0.02
		50	561	BBCH 77				< 0.01	< 0.02
		50	561	BBCH 78					
	3 (7 7)	50	1122	BBCH 75	7	Fruit	< 0.01 < 0.01	< 0.01	< 0.02
		50	1122	BBCH 77				< 0.01	< 0.02
		50	1122	BBCH 78					
Cana, VA, USA 2010 Flaming Fury	3 (7 7)	49	543	BBCH 83	7	Fruit	< 0.01 < 0.01	0.140	0.150
		52	552	BBCH 87				0.190	0.200
		50	524	BBCH 88					
Chula, GA, USA 2010 Hawthorne	3 (7 7)	50	1422	BBCH 77	7	Fruit	< 0.01 < 0.01	< 0.01	< 0.02
		53	1412	BBCH 81				< 0.01	< 0.02
		52	1384	BBCH 86					
Plains GA USA 2010 Redskin	3 (7 7)	52	655	BBCH 77	7	Fruit	< 0.01 < 0.01	< 0.01	< 0.02
		50	664	BBCH 78				< 0.01	< 0.02
		50	645	BBCH 79					
Conklin MI USA 2010 Red Haven [d]	3 (7 7)	50	580	BBCH 77	7	Fruit	< 0.01 < 0.01	0.0128	0.0228
		50	580	BBCH 78				0.0126	0.0226
		50	571	BBCH 81					
	3 (7 7)	50	1412	BBCH 77	7	Fruit	< 0.01 < 0.01	0.0256	0.0356
		50	1422	BBCH 78				0.0222	0.0322
		50	1384	BBCH 81					
D'Hanis TX 2010 Summergold [e]	3 (6 7)	52	514	BBCH 81	7	Fruit	< 0.01 < 0.01	< 0.01	< 0.02
		53	552	BBCH 85				< 0.01	< 0.02
		52	533	BBCH 85					

Location, year, variety PEACH	N (int)	Rate g ai/ha	Vol L/ha	GS application	DALA	Sample	Residues (mg/kg) Pyrifluquinazon	1H (IV-01)[b]	Sum
	3 (6 7)	52 53 52	1038 1113 1113	BBCH 81 BBCH 85 BBCH 85	7	Fruit	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Kingsburg CA USA 2010 Cling	3 (7 7)	50 50 50	571 580 580	BBCH 77 BBCH 78 BBCH 81	0	Fruit	0.0285 0.0370	0.0297 0.0266	0.0582 0.0636
					7	Fruit	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
					14	Fruit	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
					21	Fruit	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Poterville CA 2010 Fay Alberta	3 (7 7)	49 50 49	2002 2095 2039	BBCH 81 BBCH 85 BBCH 87	7	Fruit	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Dinuba CA 2010 Ivory Duchess	3 (7 7)	50 50 50	561 571 552	BBCH 81 BBCH 85 BBCH 85	7	Fruit	< 0.01 < 0.01	0.0111 < 0.01	< 0.0211 < 0.02

[a] All applications included a non-ionic surfactant

[b] Residues of 1H (IV-01) are expressed as pyrifluquinazon equivalents

[c] trials at Alton NY USA 2010 are not independent, the spray dates were the same for both trials, 13/7, 20/7 and 27/7

[d] trials at Conklin MI USA 2010 are not independent, the spray dates were the same for both trials, 6/7, 13/7 and 20/7

[e] trials at D'Hanis TX USA 2010 are not independent, the spray dates were the same for both trials, 23/6, 29/6 and 6/7

Table 57 Residues of pyrifluquinazon in plums (Wyatt 2011 R-29115)[a]

Location, year, variety PLUM	N (int)	Rate g ai/ha	Vol L/ha	GS application	DALA	Sample	Residues (mg/kg) Pyrifluquinazon	1H (IV-01)[b]	Sum
Conklin MI, USA, 2010 Stanley [c]	3 (7 7)	50 50 50	599 617 599	BBCH 83 BBCH 85 BBCH 87	7	Fruit	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
	3 (7 7)	50 50 50	1440 1496 1459	BBCH 83 BBCH 85 BBCH 87	7	Fruit	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Poplar, CA, USA, 2010 (French Prunes)[d]	3 (7 7)	50 50 49	1824 1814 1796	BBCH 78 BBCH 81 BBCH 85	7	Fruit	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
	3 (7 7)	250 252 251	1824 1814 1805	BBCH 78 BBCH 81 BBCH 85	7	Fruit	0.0150 0.0158	0.0241 0.0256	0.0391 0.0415
Dinuba, CA, USA, 2010 (Fryer's)	3 (7 7)	52 50 49	543 533 524	BBCH 81 BBCH 85 BBCH 85	0	Fruit	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
					7	Fruit	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
					14	Fruit	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
					21	Fruit	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Porterville, CA, USA, 2010 (Black Amber)	3 (7 7)	50 50 50	1833 1571 1824	BBCH 79 BBCH 85 BBCH 87	7	Fruit	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Lindsay, CA, USA, 2010 (Angelina's)	3 (7 7)	52 50 52	524 524 524	BBCH 81 BBCH 85 BBCH 85	7	Fruit	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02

Location, year, variety PLUM	N (int)	Rate g ai/ha	Vol L/ha	GS application	DALA	Sample	Residues (mg/kg) Pyrifluquinazon	1H (IV-01)[b]	Sum
Monmouth, OR, USA, 2010 (Moyer) [e]	3 (8 6)	50 52 50	636 617 617	BBCH 81 BBCH 81 BBCH 85	7	Fruit	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
	3 (8 6)	52 50 52	1291 1272 1244	BBCH 81 BBCH 81 BBCH 85	7	Fruit	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02

[a] All applications included a non-ionic surfactant

[b] Residues of 1H (IV-01) are expressed as pyrifluquinazon equivalents

[c] trials at Conklin MI USA 2010 are not independent, the spray dates were the same for both trials, 16/8, 23/8, 30/8

[d] trials at Poplar CA USA 2010 are not independent, the spray dates were the same for both trials, 26/7, 2/8, 9/8

[e] trials at Monmouth OR USA 2010 are not independent, the spray dates were the same for both trials, 26/8, 3/10, 9/10

Potato

Wyatt (2010 R-29083) conducted, sixteen residue trials on potato in the USA in 2009. In each trial pyrifluquinazon was applied three times with an interval of 14 days as a foliar spray at a nominal rate of 100 g ai/ha with a PHI of 14 days. Pyrifluquinazon was applied as a 200 g/L SC formulation. In Trial-13 a separate plot was treated at 5× the normal rate (3 × 500 g ai/ha) in order to provide samples for a processing study.

Tuber samples were analysed for residues of pyrifluquinazon and 1H (IV-01) using the analytical method No. Meth-188, rev. 3, with an LOQ of 0.01 mg/kg and LOD of 0.003 mg/kg for each analyte. Procedural recoveries were in the range of 94-116% for pyrifluquinazon (mean = 102%, n = 10, fortified at 0.01–0.1 mg/kg), and 85-120% for 1H (mean = 106%, n = 10, fortified at 0.01–0.1 mg/kg).

The samples obtained at harvest were frozen for a maximum of 111 days before extraction and analysis.

All RAC samples were received at the laboratory frozen from the field and were stored in a freezer (-20 ± 5 °C) prior to homogenization and analysis. All potato samples were ground in the presence of dry ice to a homogeneous consistency. The ground samples and subsamples were placed in frozen storage immediately after grinding and subsampling.

Table 58 Residues of pyrifluquinazon in potatoes (Wyatt 2010 R-29083) (duplicate field samples, i.e. 2 samples, one plot) [a]

Location, year, variety POTATO	N (int)	Rate g ai/ha	Vol L/ha	GS application	DALA	Sample	Residues (mg/kg) Pyrifluquinazon	1H (IV-01)[b]	Sum
Alton, NY, USA, 2009 (Superior)	3 (13 14)	102 101 102	281 281 281	BBCH 41 BBCH 43 BBCH 47	14	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Germansville, PA, USA, 2009 (Reba)	3 (14 14)	102 102 103	299 299 309	Early bud bloom Tuber set Tuber bulk	14	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Seven Springs, NC, USA, 2009 (Red Pontiac)	3 (14 15)	100 99 101	243 234 234	BBCH 51 BBCH 65 BBCH 69	13	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
O'Brien, FL, USA, 2009 (NY Red Lasodas)	3 (14 14)	102 103 100	196 187 178	BBCH 41 BBCH 44 BBCH 47	13	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Conklin, MI, USA, 2009 (Dark Red Norland	3 (14 14)	101 101 101	215 215 224	BBCH 42 BBCH 43 BBCH 47	14	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02

Location, year, variety POTATO	N (int)	Rate g ai/ha	Vol L/ha	GS application	DALA	Sample	Residues (mg/kg) Pyrifluquinazon	 1H (IV-01)[b]	 Sum
Delavan, WI, USA, 2009 (Superior)	3 (15 13)	101 100 100	206 206 196	BBCH 46 BBCH 47 BBCH 48	14	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Geneva, MN, USA, 2009 (Norland)	3 (15 14)	101 101 103	168 178 168	Flowering Post-flowering Tuber development	14	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Carrington, ND, USA, 2009 (Dark Red Norland)	3 (14 14)	103 102 105	112 112 122	BBCH 65 BBCH 69 BBCH 46 [c]	8	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
					14	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
					21	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
					28	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Dillon, MT, USA, 2009 (Norkotah Texas 278)	3 (13 14)	99 102 101	150 150 150	BBCH 43 BBCH 45 BBCH 47	14	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Porterville, CA, USA, 2009 (La Soda)	3 (14 14)	102 1001 102	150 150 150	BBCH 45 BBCH 46 BBCH 48	14	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Ephrata, WA, USA, 2009 (Umatilla)[D]	3 (14 14)	102 101 101	140 140 140	BBCH 44 BBCH 46 BBCH 47-48	14	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Ephrata, WA, USA, 2009 (Ranger Russet) [d]	3 (14 14)	101 102 102	187 187 187	BBCH 44 BBCH 46 BBCH 47+	14	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Payette, ID, USA, 2009 (Ranger Russet)	3 (15 14)	103 100 102	234 234 234	BBCH 45 BBCH 47 BBCH 48	14	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
	3 (15 14)	520 500 500	243 234 234	BBCH 45 BBCH 47 BBCH 48	14	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Minidoka, ID, USA, 2009 (Ranger Russet)	3 (16 13)	101 101 98	168 168 187	BBCH 42-44 BBCH 46-47 BBCH 91	14	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Jerome, ID, USA, 2009 (Russet Burbank)	3 (13 15)	101 102 100	187 187 196	BBCH 43 BBCH 45 BBCH 47	14	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
American Falls, ID, USA, 2009 (Russet Burbank)	3 (14 14)	102 104 100	150 150 150	BBCH 43 BBCH 44 BBCH 47	14	Tuber	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02

[a] All applications included a non-ionic surfactant

[b] Residues of 1H (IV-01) are expressed as pyrifluquinazon equivalents

[c] The BBCH growth stage is likely reported in error

[d] trials at Ephrata WA USA 2009 are independent, the crop variety is different and the spray dates were different, 5/8, 19/8 and 2/9 for one and 22/7, 5/8 and 19/8 for the other

Tree nuts

Wyatt (2010 R-29085) conducted trials on tree nuts (five on pecan and five on almond) in the USA in 2009. In each trial pyrifluquinazon was applied three times with an interval of 7 days as a foliar spray at a nominal rate of 100 g ai/ha with a PHI of 7 days. Pyrifluquinazon was applied as a 200 g/L SC formulation. All applications include a non-ionic surfactant.

Nutmeat samples were analysed for residues of pyrifluquinazon and metabolite 1H (IV-01) using the analytical method No. Meth-188, rev. 3, with an LOQ of 0.01 mg/kg and LOD of 0.003 mg/kg for each analyte. Pyrifluquinazon procedural recoveries were in the range of 86-114% in pecan nutmeat (mean=100%, n = 4, fortified at 0.01–0.5 mg/kg), 70-102% in almond nutmeat (mean=92%, n = 4, fortified at 0.01–0.5 mg/kg) and 78-96% in almond hulls (mean=88%, n = 4, fortified at 0.01-1.0 mg/kg). 1H procedural recoveries were in the range of 100-116% in pecan nutmeat (mean=106%, n = 4, fortified at 0.01–0.5 mg/kg), 84-103% in almond nutmeat (mean=97%, n = 4, fortified at 0.01–0.5 mg/kg) and 90-102% in almond hulls (mean=96%, n = 4, fortified at 0.01-1.0 mg/kg).

The samples obtained at harvest were frozen for a maximum of 84 days before extraction and analysis.

All samples were ground to a homogeneous consistency in the presence of dry ice and then placed in frozen storage immediately after grinding. Intervals between grinding and extraction were 1-29 d for pecan nutmeat and 5-29 d for almond nutmeat and hulls.

Table 59 Residues of pyrifluquinazon in pecans (Wyatt 2010 R-29085) (duplicate samples same field plot)[a]

Location, year, variety PECAN	N (int)	Rate g ai/ha	Vol L/ha	GS application	DALA	Sample	Residues (mg/kg) Pyrifluquinazon	1H (IV-01)[b]	Sum
Girard, GA, USA, 2009 (Desirable)	3 (7 7)	103 101 101	1169 1188 1225	BBCH 85 BBCH 87 BBCH 89	7	Nutmeat	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Montezuma, GA, USA, 2009 (Cape Fear)	3 (7 6)	101 102 101	1384 1375 1300	BBCH 85 BBCH 87 BBCH 89	7	Nutmeat	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Alexandria, LA, USA, 2009 (Creek)	3 (6 7)	103 103 102	1824 1927 1936	Shuck split Shuck split/hulls browning Shucks hard/open	7	Nutmeat	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Pearsall, TX, USA, 2009 (Wichita)	3 (7 7)	102 101 101	589 561 561	BBCH 85 BBCH 85 BBCH 87	0	Nutmeat	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
					7	Nutmeat	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
					14	Nutmeat	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
					21	Nutmeat	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Anton, TX, USA, 2009 (Western Schley)	3 (7 7)	100 102 100	645 664 655	Shuck split/some green Start shuck split/mature Shuck split	7	Nutmeat	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02

[a] All applications included a non-ionic surfactant

[b] Residues of 1H (IV-01) are expressed as pyrifluquinazon equivalents

Table 60 Residues of pyrifluquinazon in almonds (Wyatt 2010 R-29085) [a]

Location, year, variety ALMOND	N (int)	Rate g ai/ha	Vol L/ha	GS application	DALA	Sample	Residues (mg/kg) Pyrifluquinazon	1H (IV-01)[b]	Sum
Terra Bella, CA, USA, 2009 (Monterey)	3 (7 7)	102 101 101	524 664 636	BBCH 81 BBCH 81 BBCH 87	0	Nutmeat	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
					7	Nutmeat	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
					14	Nutmeat	< 0.01	< 0.01	< 0.02

Location, year, variety ALMOND	N (int)	Rate g ai/ha	Vol L/ha	GS application	DALA	Sample	Residues (mg/kg) Pyrifluquinazon	1H (IV-01) [b]	Sum
							< 0.01	< 0.01	< 0.02
					21	Nutmeat	< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	< 0.02
Dinuba, CA, USA, 2009 (Non-Pareil)	3 (7 7)	1001 100 101	1805 1730 1674	BBCH 85 BBCH 86 BBCH 88	7	Nutmeat	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Wasco, CA, USA, 2009 (Price)	3 (7 7)	101 101 101	617 655 664	BBCH 82 BBCH 82 BBCH 84-86	7	Nutmeat	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Strathmore, CA, USA, 2009 (Fritz)	3 (7 7)	102 101 101	1440 1375 1459	BBCH 81 BBCH 81 BBCH 82	7	Nutmeat	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02
Hanford, CA, USA, 2009 (Padre)	3 (7 7)	102 101 100	664 655 505	BBCH 81 BBCH 85 BBCH 89	7	Nutmeat	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 < 0.02

[a] All applications included a non-ionic surfactant

[b] Residues of 1H (IV-01) are expressed as pyrifluquinazon equivalents

Tea

In total, eight residue trials were conducted on tea in Japan from 2004 to 2007. Trials were conducted where pyrifluquinazon was applied twice with a retreatment interval of 7 days as a foliar spray at a nominal rate of 1 × 1000 g ai/ha + 1 × 400 g ai/ha, with a PHI of 7 days. In all trials pyrifluquinazon was applied as a 20% WG formulation. In two trials the application rates were c. 667 and 133 g ai/ha.

Tea leaves were collected 1/3, 7 and 14 days after the last application (R-29046, R-29049, R-29050) and 7 days after the last application (R-26069). The leaves were processed in a manner reflecting commercial green tea production. The fresh green tea leaves were processed with a Yagi-type Process Tea Machine to produce dried green tea.

Samples of dried green tea leaves were analysed for residues of pyrifluquinazon and metabolite 1H (IV-01) using the analytical methods described and validated within the residue reports, with an LOQ of 0.05 mg/kg and LOD of 0.025 mg/kg for each analyte.

R-29049: Procedural recoveries were in the range of 82–93% for pyrifluquinazon (mean=90%, n = 12, fortified at 0.05–20 mg/kg), and 88–95% for 1H (mean = 92%, n = 12, fortified at 0.05–20 mg/kg).

R-29050: Procedural recoveries were in the range of 93-114% for pyrifluquinazon (mean=104%, n = 12, fortified at 0.05–20 mg/kg), and 94–119% for 1H (mean=107%, n = 12, fortified at 0.05–20 mg/kg).

R-29069: Procedural recoveries were in the range of 93-110% for pyrifluquinazon (mean=102%, n = 24, fortified at 0.05–6 mg/kg), and 89–120% for 1H (mean=107%, n = 24, fortified at 0.05–5 mg/kg).

Samples obtained at harvest were shipped on the same day to the laboratory under cold storage conditions and were extracted and analysed immediately on arrival at the laboratory.

Table 61 Residues of pyrifluquinazon in green tea (Wyatt 2010 R-29085)[a]

Location, year, variety TEA	N (int)	Rate g ai/ha	Spray conc g ai/hL	GS application	DALA	Sample	Residues (mg/kg) Pyrifluquinazon	1H (IV-01)[b]	Sum
Kikugawa-shi, Shizuoka, Japan, 2006 (Yabukita) (29049)	2 (7)	1000 400	10 10	2-3 leaf stage 3-4 leaf stage	3	Dried tea	18.7 18.5	11.0 10.9	29.6
Analysis lab 1	2 (7)	1000 400	10 10	1.5-2 leaf stage 2.5-3 leaf stage	7	Dried tea	8.77 8.68	5.70 5.60	14.4
	2 (7)	1000 400	10 10	0.5-1 leaf stage 1.5-2 leaf stage	14	Dried tea	0.16 0.15	0.385 0.374	0.5
(29050)	2 (7)	1000 400	10 10	2-3 leaf stage 3-4 leaf stage	3	Dried tea	18.4 18.2	11.5 11.4	29.7
Analysis lab 2	2 (7)	1000 400	10 10	1.5-2 leaf stage 2.5-3 leaf stage	7	Dried tea	7.58 7.52	5.12 5.07	12.7
	2 (7)	1000 400	10 10	0.5-1 leaf stage 1.5-2 leaf stage	14	Dried tea	0.11 0.10	0.264 0.253	0.4
Average lab 1+lab2					3 7 14	Dried tea	18.45 8.14 0.13	11.2 5.37 0.319	29.65 <u>13.51</u> 0.449
Minami-Kyushu-shi, Kagoshima, Japan, 2006 (Okumidori) (29049)	2 (7)	1000 200	10 10		3	Dried tea	7.79 7.69	10.1 9.93	17.7
Analysis lab 1	2 (7)	1000 200	10 10		7	Dried tea	1.94 1.90	2.75 2.74	4.7
	2 (7)	1000 200	10 10		14	Dried tea	0.06 0.06	0.154 0.154	0.2
(29050)	2 (7)	1000 200	10 10		3	Dried tea	8.62 8.46	12.2 11.9	20.5
Analysis lab 2	2 (7)	1000 200	10 10		7	Dried tea	2.40 2.40	3.21 3.20	5.6
	2 (7)	1000 200	10 10		14	Dried tea	0.08 0.07	0.121 0.121	0.2
Average lab 1+lab2					3 7 14	Dried tea	8.14 2.16 0.068	11.03 2.98 0.138	19.17 <u>5.14</u> 0.206
Iruma-shi, Saitama, Japan, 2007 (Yabukita) (29069)	2 (7)	1029 411	10.3 10.3		7	Dried tea	2.78 2.49	3.27 2.84	<u>5.7</u>
Nara-shi, Nara, Japan, 2007 (Yabukita) (29069)	2 (7)	1000 400	10 10		7	Dried tea	1.15 1.05	1.48 1.39	<u>2.53</u>
Agawa-gun, Kochi, Japan, 2007 (Yabukita) (29069)	2 (7)	1000 400	10 10		7	Dried tea	1.95 1.94	4.17 4.11	<u>6.07</u>
Kamimashiki-gun, Kumamoto, Japan, 2007 (Okumidori) (29069)	2 (7)	1000 400	10 10		7	Dried tea	0.26 0.26	0.957 0.935	<u>1.21</u>
Uji-shi, Kyoto, Japan 2004 Yabukita (29046)	2 (9)	667 136	6.7 6.8	4.0 leaf stage 5.0 leaf stage	1	Dried tea	35.3 33.9	10.8 10.4	45.2
	2 (7)	667 136	6.7 6.8	4.0 leaf stage 4.5 leaf stage	3	Dried tea	1.00 0.97	1.14 1.17	2.1
	2 (7)	667 136	6.7 6.8	3.5 leaf stage 4.5 leaf stage	7	Dried tea	0.28 0.25	0.30 0.33	0.6
	2 (6)	667 136	6.7 6.8	2.0 leaf stage 2.5 leaf stage	14	Dried tea	0.09 0.09	0.11 0.11	0.2
Agawa-gun, Kochi, Japan 2004 Yabukita (29046)	2 (7)	667 133	6.7 6.7	First flush First flush	1	Dried tea	28.1 27.5	8.98 9.15	36.9
	2 (7)	667	6.7	First flush	3	Dried tea	4.60 4.45	2.01 1.96	6.5

Location, year, variety TEA	N (int)	Rate g ai/ha	Spray conc g ai/hL	GS application	DALA	Sample	Residues (mg/kg) Pyrifluquinazon	1H (IV-01)[b]	Sum
		133	6.7	First flush					
	2 (7)	667 133	6.7 6.7	First flush First flush	7	Dried tea	2.23 2.16	1.14 1.10	3.3
	2 (7)	667 133	6.7 6.7	First flush First flush	14	Dried tea	0.47 0.47	0.30 0.31	0.8

[a] All applications included a non-ionic surfactant

[b] parent compound equivalents. The conversion factor = 1.0996 = molecular weight of pyrifluquinazon (464.34)/molecular weight of deacetylated pyrifluquinazon (422.30).

ANIMAL FEED COMMODITIES

Almond Hulls

Table 62 Residues of pyrifluquinazon in almond hulls (Wyatt 2010 R-29085)[A]

Location, year, variety ALMOND HULLS	N (int)	Rate g ai/ha	Vol L/ha	GS application	DALA	Sample	Residues (mg/kg) Pyrifluquinazon	1H (IV-01)[B]	Sum
Terra Bella, CA, USA, 2009 (Monterey) 80.6% moisture	3 (7 7)	102 101 101	524 664 636	BBCH 81 BBCH 81 BBCH 87	0	Hulls	0.288 0.278	0.0654 0.0558	0.353 0.333
					7	Hulls	0.0842 0.102	0.0272 0.0197	0.111 0.122
					14	Hulls	0.122 0.0855	0.0260 0.0163	0.148 0.102
					21	Hulls	0.105 0.163	0.0142 0.0292	0.119 0.192
Dinuba, CA, USA, 2009 (Non-Pareil) (20.8% moist)	3 (7 7)	1001 100 101	1805 1730 1674	BBCH 85 BBCH 86 BBCH 88	7	Hulls	0.260 0.282	0.0531 0.0558	0.314 0.337
Wasco, CA, USA, 2009 (Price) (26.6% moist)	3 (7 7)	101 101 101	617 655 664	BBCH 82 BBCH 82 BBCH 84-86	7	Hulls	0.452 0.422	0.0795 0.0550	0.531 0.477
Strathmore, CA, USA, 2009 (Fritz) (73.1% moist)	3 (7 7)	102 101 101	1440 1375 1459	BBCH 81 BBCH 81 BBCH 82	7	Hulls	0.202 0.146	0.0591 0.0605	0.261 0.207
Hanford, CA, USA, 2009 (Padre) (26.1% moist)	3 (7 7)	102 101 100	664 655 505	BBCH 81 BBCH 85 BBCH 89	7	Hulls	0.520 0.446	0.0825 0.0627	0.602 0.509

[a] All applications included a non-ionic surfactant

[b] Residues of 1H (IV-01) are expressed as pyrifluquinazon equivalents

FATE OF RESIDUES DURING PROCESSING

Effects on the Nature of the Residues during Processing

A study on the nature of residues during simulated processing was not available to the Meeting.

The Meeting received trials on the processing of plums, potato and tea.

Plums

Wyatt 2011 (2011 R-29115) conducted a study on the residue behaviour of pyrifluquinazon in plums and their processed products. A plum field trial was performed in the USA during the 2010 growing

season using an SC formulation to obtain plum fruit for a processing study. There were three foliar applications at a nominal rate of 250 g ai/ha (5× the GAP rate). The spray volumes were in the range of 1805-1824 L/ha. The interval between subsequent applications was 7 days and the last application was conducted 7 days before harvest.

Processing of plums approximated commercial practices. Fruit for processing (24.7 kg) were washed (2 kg cold water to 1 kg fruit for 5 min) and placed in a MLSM Laboratory Tray Air Dryer set at 74 °C. The fruit were dried until a moisture content of < 33% was obtained. Prunes were then cooled and frozen.

Samples were analysed for residues of pyrifluquinazon and its metabolite 1H (IV-01) using analytical method No. Meth-188, rev. 3, with an LOQ of 0.01 mg/kg and LOD of 0.003 mg/kg for each analyte. Procedural recoveries were in the range of 92–96% for parent pyrifluquinazon (mean=94%, n = 2, fortified at 0.01–1.0 mg/kg) and in the range of 94–99% for 1H (mean=96%, n = 2, fortified at 0.01–1.0 mg/kg). Prune samples were analysed within 34 days of processing.

Table 63 Calculation of the processing factors in processed fractions of plum at 7 DAT

Trial	Commodity/Processed Fraction	Pyrifluquinazon	1H, expressed as pyrifluquinazon	Sum	Processing Factors [a]
R-29115, Trial: TCI-10-259-17	Plum fruit (RAC)	0.0150; 0.0158 (0.0154)	0.0241; 0.0256 (0.0249)	0.0391; 0.0415 (0.0403)	-
Poplar, CA, USA, 2010 (French Prunes)	Prunes	0.0188; 0.0230 (0.0209)	0.0377; 0.0404 (0.0391)	0.0564; 0.0634 (0.0599)	1.5

[a] Processing factor = residue level in processed commodity (mg/kg) ÷ residue level in RAC (mg/kg)

Residues of pyrifluquinazon and 1H (IV-01) are concentrated in prunes with a processing factor of 1.5 for the sum of pyrifluquinazon and IV-01.

Potato

A potato field trial was performed in the USA during the 2009 growing season using an SC formulation to obtain potato tubers for a processing study. There were three foliar applications at a nominal rate of 500 g ai/ha (5× the GAP rate). The spray volumes were in the range of 234–243 L/ha. The interval between subsequent applications was 14 days and the last application was conducted 14 days before harvest.

Processing of potato tubers approximated commercial practices. Tubers for processing for potato flakes (29 kg) were washed, steam peeled (45 sec, ≈100–120 psi), scrubbed (30 sec, Hobart peeler) and hand trimmed to remove additional peel, rot, green or otherwise damaged potatoes. The potato peel from the peeling, scrubbing and trimming process was combined and pressed and a representative sample taken (potato wet peel). The peeled potatoes were sliced, spray washed (30 sec, cold water), pre-cooked (70–77 °C for 21 min), steam cooked (94–100 °C for 40–42 min), mashed and dried in an Overton Single Drum Dryer to generate a thin sheet. A fruit press hammermill uniformly milled the sheet into potato flakes. The moisture content was ≤ 9%. For potato chips, tubers (11.5 kg) were washed, peeled (25–35 sec, abrasive peeler), sliced, blanched and fried (163–191 °C for ≈120 sec).

Samples were analysed for residues of pyrifluquinazon and its metabolite 1H (IV-01) using analytical method No. Meth-188, rev. 3, with an LOQ of 0.01 mg/kg and LOD of 0.003 mg/kg for each analyte.

Pyrifluquinazon procedural recoveries were in the range of 99-118% in potato flakes (mean = 108%, n = 2, fortified at 0.01–0.1 mg/kg), 114-120% in potato chips (mean = 117%, n = 2, fortified at 0.01–0.1 mg/kg) and 106-108% in wet peel (mean = 107%, n = 2, fortified at 0.01–0.1 mg/kg). 1H procedural recoveries were in the range of 100-116% in potato flakes (mean = 108%,

n = 2, fortified at 0.01–0.1 mg/kg), 102-118% in potato chips (mean = 110%, n = 2, fortified at 0.01–0.1 mg/kg) and 99-110% in wet peel (mean = 104% n = 2, fortified at 0.01–0.1 mg/kg). The processed potato fractions were stored frozen for a maximum of 16 days before extraction and analysis.

Calculations of processing factors are presented in Table 64.

Table 64 Calculation of the processing factors in processed fractions of potato at 14 DALA

Trial	Commodity/Processed Fraction	Pyrifluquinazon	1H, expressed as pyrifluquinazon	Sum	Processing Factors
R-29083, Trial: TCI-09-236-13, Payette, ID, USA, 2009 (Ranger Russet)	Potato tuber (RAC)	< 0.01	< 0.01	< 0.02	-
	Potato flakes	< 0.01	< 0.01	< 0.02	-
	Potato chips	< 0.01	< 0.01	< 0.02	-
	Potato wet peel	< 0.01	< 0.01	< 0.02	-

As residues of both the parent and metabolite were not detected in the RAC and all processed samples, no processing factor can be derived.

Tea

A processing study on tea has been performed (Miyahana 2006 R-29051) Two field trials (study R-29049, see section 6.4) were conducted in Japan during 2006. Tea was treated twice with pyrifluquinazon as a 20% w/w WG formulation at nominal rates of 1 × 1000 g ai/ha + 1 × 400 g ai/ha.

Samples of tea leaves were collected 3, 7 and 14 days after treatment and processed in a manner approximating commercial green tea production. The fresh green tea leaves were first steamed for 30 seconds and then processed with Yagi-type Process Tea Machine to produce dried green tea, which was further dried in a shelf drier for 60 min at 60 °C. The dried green tea was infused in hot water at 100 °C for 5 minutes then filtered before sampling for analysis.

The infusion was analysed for residues of pyrifluquinazon and 1H (IV-01) by LC MS. Procedural recoveries were in the range of 90-114% for pyrifluquinazon (mean=100%, n = 12, fortified at 0.05-2 mg/kg), and 99-115% for 1H (IV-01) (mean = 105%, n = 12, fortified at 0.05-2 mg/kg). Samples were analysed immediately on arrival at the laboratory. Calculations of processing factors are presented in Table 65.

Table 65 Calculation of the processing factors in green tea infusion [a]

Trial	Matrix	Pyrifluquinazon			1H, expressed as pyrifluquinazon			Sum			Processing Factors		
DALA		3	7	14	3	7	14	3	7	14	3	7	14
Tea R-29049/ R-29050, Trial: Shizuoka, Kikugawa-shi, Shizuoka, Japan, 2006 (Yabukita) R-29051	Green tea, dried	18.4 18.2 (18.3)	7.58 7.52 (7.55)	0.11 0.10 (0.105)	11.5 11.4 (11.5)	5.12 5.07 (5.10)	0.264 0.253 (0.259)	29.8	12.6	0.36	-	-	-
	Green tea infusion	0.0285 0.0282 (0.0284)	0.0225 0.0222 (0.0224)	0.0013 0.0013 (0.0013)	0.0137 0.0135 (0.0136)	0.0110 0.0108 (0.0109)	0.0011 0.0011 (0.0011)	0.042	0.033	0.002	0.0001	0.0026	0.0056
Tea R-29049/ R-29050, Trial: Kagoshima, Minami-Kyushu-shi, Kagoshima, Japan, 2006 (Okumidori) R-29051	Green tea, dried	8.62 8.46 (8.54)	2.40 2.40 (2.40)	0.08 0.07 (0.08)	12.2 11.9 (12.1)	3.21 3.20 (3.21)	0.121 0.121 (0.121)	20.6	5.6	0.201	-	-	-
	Green tea infusion	0.0213 0.0202 (0.0208)	0.0055 0.0053 (0.0054)	< 0.0009 < 0.0009 (< 0.0009)	0.0178 0.0168 (0.0174)	0.0046 0.0044 (0.0045)	< 0.0010 < 0.0010 (< 0.0010)	0.038	0.010	< 0.002	0.0018	0.0018	0.0100

Trial	Matrix	Pyrifluquinazon			1H, expressed as pyrifluquinazon			Sum			Processing Factors		
DALA		3	7	14	3	7	14	3	7	14	3	7	14
Median/Mean PF											0.0010	0.0022	0.0078

[a] The test facility that conducted the analysis on the infusion was analytical lab 2, therefore the residues in the RAC as determined analytical lab 2 are used for the determination of a processing factor.

Residues of pyrifluquinazon and 1H (IV-01) are not concentrated in tea infusion.

A summary of relevant pyrifluquinazon processing factors is provided below (Table 66).

Table 66 Pyrifluquinazon processing factors obtained from plum and tea processing studies

Commodity	Individual Processing Factors	Mean PF
Prune	1.5	-
Tea infusion (7 DALA)	0.0018 0.0026	0.0022

Livestock feeding studies

Dairy cow feeding studies

The transfer of pyrifluquinazon from feed to tissues and milk of dairy cows was studied by Cremin and Arndt (2012 R-29123). Three groups of three Holstein cows (3-5 years old, 450-586 kg bw) were dosed orally via gelatine capsules with pyrifluquinazon at doses equivalent to 0.5, 1.5 and 5.1 ppm for 28 days (0.02, 0.04 and 0.15 mg/kg bw). An additional three animals were dosed at the high rate and were used for the depuration phase of the study.

Feed consumption was approximately 5.1 kg grain, 3.6 kg baled hay, 8.2-8.4 kg corn silage with average dry-weight feed consumed 16.9, 17.0 and 16.7 kg/day for the three dose groups respectively.

Mean daily milk yields for the dose groups during were 18 to 22 kg/cow/day. Milk was collected twice daily (am and pm sampling and pooled in a ratio reflecting production. Milk from days 13 and 28 was separated into cream and skim milk for the control group and the 0.5 and 5.1 ppm groups. Muscle (loin, leg), liver, kidney and fat (perirenal, subcutaneous, omental) were collected at sacrifice 24 hours after the last dose.

All samples were stored frozen and homogenised under cryogenic (dry ice) conditions. The maximum frozen storage interval for tissue and milk samples was 49 days. Analysis was carried out according to method A-29022 for the determination of pyrifluquinazon and metabolites IV-01, IV-03, IV-04, IV-15, IV-203 and IV-208. The LOQ of the methods was 0.005 mg/kg for milk and 0.01 mg/kg for tissues.

No residues of pyrifluquinazon or metabolites IV-04 or IV-203 above the LOQ of 0.005 mg/kg were detected at any timepoint in the 0.5 and 1.5 ppm diet treatment groups. In the highest treatment group (5.1 ppm diet) residues of pyrifluquinazon and IV-203 were <LOQ, but positive residues of IV-04 were detected between 0.005 and 0.008 mg/kg. No residues of pyrifluquinazon or IV-04 or IV-203 in were detected in skim milk above the LOQ. In cream samples all residues were < LOQ, apart from the day 13 and 28 samples of cream in the highest treatment group (5.1 ppm diet), which were detected at 0.005 mg/kg.

Table 67 Mean residues of pyrifluquinazon, IV-04 and IV-203 in milk, skim milk and cream [a]

Day	5.1 ppm		
	Pyrifluquinazon	IV-04	IV-203
-1	< 0.005	< 0.005	< 0.005

Day	5.1 ppm		
	Pyrifluquinazon	IV-04	IV-203
1	< 0.005	< 0.005	< 0.005
2	< 0.005	0.007	< 0.005
3	< 0.005	0.007	< 0.005
4	< 0.005	0.006	< 0.005
5	< 0.005	0.007	< 0.005
6	< 0.005	0.008	< 0.005
7	< 0.005	0.007	< 0.005
10	< 0.005	0.008	< 0.005
13	< 0.005	0.007	< 0.005
16	< 0.005	0.006	< 0.005
19	< 0.005	0.005	< 0.005
22	< 0.005	0.005	< 0.005
25	< 0.005	0.007	< 0.005
28	< 0.005	< 0.005	< 0.005
+3	< 0.005	< 0.005	< 0.005
+7	< 0.005	< 0.005	< 0.005
+14	< 0.005	< 0.005	< 0.005
Skim milk			
13	< 0.005	< 0.005	< 0.005
28	< 0.005	< 0.005	< 0.005
Cream			
13	< 0.005	0.005	< 0.005
28	< 0.005	0.005	< 0.005

[a] Residues are an average of three replicates

In milk, residues of pyrifluquinazon, IV-04 and IV-203 were measured. No residues of pyrifluquinazon or IV-203 above the LOQ of 0.005 mg/kg were detected in any sample. In the 5.1 ppm group residues of IV-04 were detected between 0.005 and 0.008 mg/kg. No residues of pyrifluquinazon or IV-04 or IV-203 in were detected in skim milk above the LOQ. In cream samples all residues were < LOQ, apart from the day 13 and 28 samples of cream in the highest treatment group (5.1 ppm diet), which were detected at 0.005 mg/kg.

In tissues, residues of pyrifluazuron, IV-01, IV-03, IV-15, IV-203 and IV-208 were measured. The only residues detected were IV-01 in liver, at mean levels of < 0.011 (max 0.013), 0.026 (max 0.034) and 0.062 (max 0.074) mg/kg for the 0.5, 1.5 and 5.1 ppm dose groups respectively, IV-01 in kidney of the 5.1 ppm dose group at a mean level of < 0.01 (max 0.01) mg/kg and IV-203 in liver of the 5.1 ppm dose group at a mean level of 0.011 (max 0.013) mg/kg.

Table 68 Residues of pyrifluquinazon, IV-01, IV-03, IV-15, IV-203 and IV-208 in bovine tissues [a]

Tissue	5.1 ppm diet					
	Pyrifluquinazon	IV-01	IV-03	IV-15	IV-203	IV-208
Day 28						
Liver	< 0.01 (3)	0.063 0.049 0.074	NA	< 0.01 (3)	0.011 < 0.01 0.013	NA
Kidney	< 0.01 (3)	< 0.01 < 0.01 0.01	< 0.01 (3)	< 0.01 (3)	< 0.01 (3)	NA
Loin muscle	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)
Leg muscle	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)
Subcutaneous fat	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)
Perirenal fat	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)

Tissue	5.1 ppm diet					
	Pyrifluquinazon	IV-01	IV-03	IV-15	IV-203	IV-208
Omental fat	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)
+3 days						
Liver	< 0.01 (3)	< 0.01 (3)	NA	0.011 < 0.01 < 0.01	< 0.01 (3)	NA
Kidney	< 0.01 (3)	< 0.01 (3)	< 0.01 (3)	< 0.01 (3)	< 0.01 (3)	NA
Loin muscle	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)
Leg muscle	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)
Subcutaneous fat	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)
Perirenal fat	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)
Omental fat	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)
+7 days						
Liver	< 0.01 (3)	< 0.01 (3)	NA	< 0.01 (3)	< 0.01 (3)	NA
Kidney	< 0.01 (3)	< 0.01 (3)	< 0.01 (3)	< 0.01 (3)	< 0.01 (3)	NA
Loin muscle	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)
Leg muscle	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)
Subcutaneous fat	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)
Perirenal fat	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)
Omental fat	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)
+14 days						
Liver	< 0.01 (3)	< 0.01 (3)	NA	< 0.01 (3)	< 0.01 (3)	NA
Kidney	< 0.01 (3)	< 0.01 (3)	< 0.01 (3)	< 0.01 (3)	< 0.01 (3)	NA
Loin muscle	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)
Leg muscle	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)
Subcutaneous fat	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)
Perirenal fat	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)
Omental fat	< 0.01 (3)	NA	NA	NA	< 0.01 (3)	< 0.01 (3)

[a] Residues are an average of three replicates

NA Not analysed

Residues of IV-01 were also detected in liver of the 0.5 ppm (0.013, < 0.01, < 0.01 mg/kg) and 1.5 ppm dose groups (0.034, 0.020, 0.024 mg/kg).

International residue definitions

Japan:

The sum of pyrifluquinazon and metabolite B,1,2,3,4-tetrahydro-3-[(3-pyridinylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazoline-2-one, expressed as pyrifluquinazon.quinazoline-2-one calculated as pyrifluquinazon.

Republic of Korea

Pyrifluquinazon

Taiwan

Pyrifluquinazon

USA:

§180.701 Pyrifluquinazon; tolerances for residues.

Plant commodities

(1) Tolerances are established for residues of the insecticide pyrifluquinazon, including its metabolites and degradates, in or on the commodities in the table below. Compliance with the tolerance levels specified below is to be determined by measuring only the sum of pyrifluquinazon (1-acetyl-3,4-dihydro-3-[(3-pyridinylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]-2(1H)-quinazolinone) and its metabolite IV-01 (3-[(pyridin-3-ylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]-3,4-dihydro-1H-quinazolin-2-one), calculated as the stoichiometric equivalent of pyrifluquinazon.

Livestock commodities

(2) Tolerances are established for residues of the insecticide pyrifluquinazon, including its metabolites and degradates, in or on liver. Compliance with the tolerance levels specified below is to be determined by measuring only the sum of pyrifluquinazon (1-acetyl-3,4-dihydro-3-[(3-pyridinylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]-2(1H)-quinazolinone) and the free and conjugated forms of its metabolites IV-01 (3-[(pyridin-3-ylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]-3,4-dihydro-1H-quinazolin-2-one) and IV-203 (6-[1,2,2,2-tetrafluoro-1-trifluoromethyl)ethyl]-1H-quinazolin-2,4-dione), calculated as the stoichiometric equivalent of pyrifluquinazon

Table 69 Summary of metabolites and degradates to be included in the risk assessment and tolerance expression

Matrix		Residues Included in Risk Assessment	Residues Included in Tolerance Expression
Plants	Primary Crops	Pyrifluquinazon + IV-01	Pyrifluquinazon + IV-01
	Rotational Crops	Pyrifluquinazon + IV-203[a]	Pyrifluquinazon + IV-203[a]
Livestock	Ruminant Tissues	Pyrifluquinazon + IV-01[a] + IV-203[a]	Pyrifluquinazon + IV-01[a] + IV-203[a]
	Milk	Pyrifluquinazon + IV-203 + IV-04	Pyrifluquinazon + IV-203 + IV-04
	Poultry	Pyrifluquinazon + IV-203[a] + IV-208	To be determined

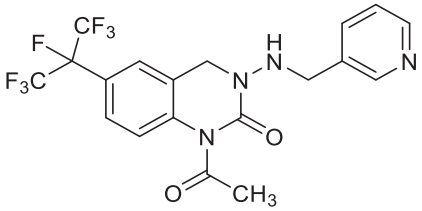
[a] Includes free and conjugated forms.

APPRAISAL

Pyrifluquinazon is a non-systemic insecticide for the control of sap-feeding insects. It acts by modification of insect feeding behaviour. Pyrifluquinazon was scheduled at the Fiftieth Session of the CCPR for evaluation as a new compound by the 2019 JMPR.

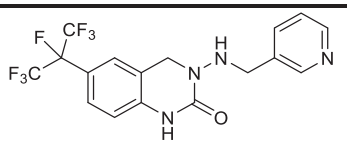
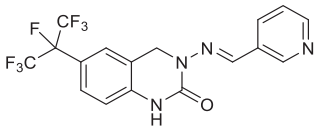
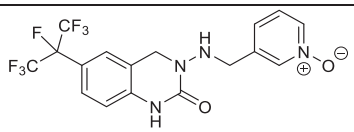
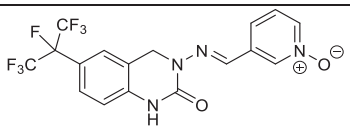
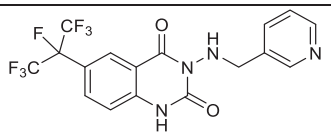
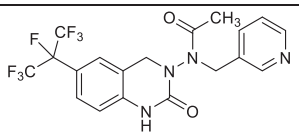
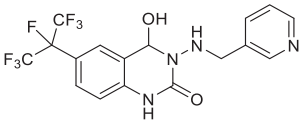
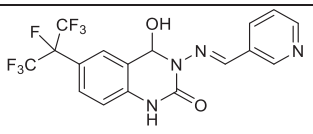
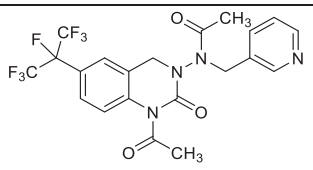
The Meeting received information on the identity, physicochemical properties, metabolism of pyrifluquinazon in plants and livestock, rotational crops, methods of residue analysis, freezer storage stability, GAP information, supervised residue trials on stone fruit (cherries, peaches, plums), potato, tea and tree nuts (almonds, pecans) as well as a livestock feeding study (lactating cow).

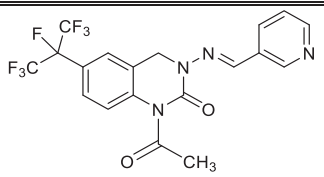
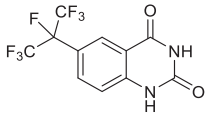
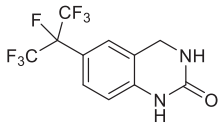
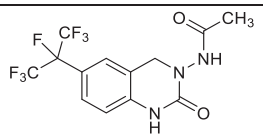
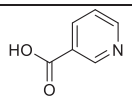
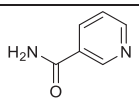
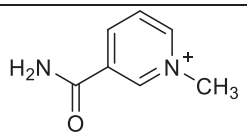
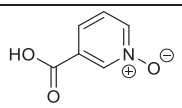
Pyrifluquinazon is 1-acetyl-1,2,3,4-tetrahydro-3-[(3-pyridylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2-one.



The following abbreviations are used for the major metabolites discussed below:

Table 1 Abbreviations used for the major metabolites

Code	Name	Structure
1H IV-01	1,2,3,4-tetrahydro-3-[(3-pyridylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2-one	
1H-imino IV-02	1,2,3,4-tetrahydro-3-[(3-pyridylmethylene)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2-one	
1H-oxide IV-03	1,2,3,4-tetrahydro-3-[3-(1-oxy-pyridylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2-one	
1H-imino-oxide IV-04	1,2,3,4-tetrahydro-3-[3-(1-oxy-pyridylmethylene)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2-one	
1H-4-oxo IV-15	1,2,3,4-tetrahydro-3-[3-pyridylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2,4-dione	
1H-N-Ac IV-17	*N*-[2-oxo-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]-1,4-dihydro-2Hquinazolin-3-yl]-*N*-(Pyr-3-ylmethyl) Acetamide	
1H-4-OH IV-27	1,2,3,4-tetrahydro-4-hydroxy-3-[3-(pyridylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2-one	
1H-inmino-4-OH IV-28	4-hydroxy-3-[(pyridine-3-ylmethylene)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]-3,4-dihydro-1*H*-quinazolin-2-one	
N-Ac IV-101	*N*- [1-acetyl-2-oxo-6- [1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]- 1,4-dihydro-2*H*-quinazolin-3-yl] -*N*-(pyridin-3-ylmethyl) acetamide	

Code	Name	Structure
Imino IV-102	l-acetyl-3- [(pyridin-3-ylmethylene)amino]-6- [1,2,2,2-tetrafluoro- l-(trifluoromethyl)ethyl] -3,4-dihydro-1*H*-quinazolin-2-one	
quinazolinedione IV-203	1,2,3,4-tetrahydro-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2,4-dione	
quinazolinone IV-206	6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]-3,4-dihydro-1*H*-quinazolin-2-one	
aminoquinazolinone-N-Ac IV-208	*N*-[2-oxo-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]-1,4-dihydro-2*H*-quinazolin-3-yl]acetamide	
Nicotinic acid (niacin) IV-403	Pyridine-3-carboxylic acid	
Nicotinamide (niacinamide) IV-404	Pyridine-3-carboxylic acid amide	
Methyl-nicotinamide IV-405	3-carbamoyl-1-methylpyridinium	
Nicotinic acid N-oxide	Nicotinic acid *N*-oxide	

With respect to the physical and chemical properties of pyrifluquinazon that may impact on residues in crops and livestock, pyrifluquinazon is potentially fat soluble (log P_{ow} >3), not volatile, stable to hydrolysis at physiological pH and can be degraded via photolysis.

The metabolism of pyrifluquinazon in plants, animals and soils was investigated using [quinazolinone-phenyl-U-^{14}C]-pyrifluquinazon (Qn-label) and [pyridine-2,6-^{14}C]-pyrifluquinazon (Pyr-label).

Plant metabolism

The Meeting received studies on the metabolism of pyrifluquinazon after foliar application to tomato (fruiting vegetables other), lettuce (leafy vegetables) and radish (root & tuber vegetables). Plants were maintained in a greenhouse with a UV transparent quartz ceiling.

Tomato

The metabolic fate of [^{14}C]- pyrifluquinazon in tomato plants maintained in a greenhouse was examined following three foliar applications of 0.1 kg ai/ha each made at 7 day intervals with an WDG formulation. Fruit and leaves were harvested at 0, 1, 7 and 14 days after the last application.

TRRs in rank order were 0.05–0.16 mg eq/kg in roots, 0.67-1.3 mg eq/kg in stems, 0.41–0.76 mg eq/kg in fruit and 13–21 mg eq/kg in leaves.

The majority of ^{14}C residues in fruit and leaves were associated with surface rinses (acetonitrile/H_2O rinse 49–80% TRR). Extractability of ^{14}C residues with the solvent system (acetonitrile/H_2O, acetonitrile) used was >71% in fruit (71–90% TRR), >83% in leaves (83–94% TRR) and > 45% from roots (45–51% TRR).

Parent pyrifluquinazon was the major component observed in all samples from 0 to 14 DALA. In fruits, pyrifluquinazon ranged from 42% TRR (0.17 mg/kg) at 7 DALA to 72% TRR (0.55 mg/kg) at 1 DALA. In leaves, pyrifluquinazon ranged from 46% TRR (9.4 mg/kg) at 14 DALA to 72% TRR (13 mg/kg) at 1 DALA. Metabolite 1H (IV-01) was detected in fruits at a maximum of 11% TRR (0.039 mg eq/kg) at 0 DALA and in leaves at a maximum of 9.8% TRR (1.3 mg eq/kg) at 0 DALA.

Further metabolites were detected at low levels (<10% TRR); 1H-imino (IV-02), 1H-oxide (IV-03), 1H-imino-oxide (IV-04), 1H-4-oxo (IV-15), 1H-N-Ac (IV-17), N-Ac (IV-101), imino (IV-102), quinazolinedione (IV-203) and quinazolinone (IV-206).

PES accounted for 21 to 29% TRR in fruit at 14 DALA of which 4.8-7.8% TRR was associated with lignins.

Lettuce

In a metabolism study on head lettuce, three foliar applications of a WG formulation were made at 0.2 kg ai/ha and at seven day intervals to lettuce plants grown in a greenhouse with harvest 0-14 days after the last application.

At 14 DALA, TRRs were lowest in roots (0.06 to 0.10 mg eq/kg), higher in stems (0.23–0.30 mg eq/kg) and heads (0.56-1.4 mg eq/kg) and the highest in outer leaves (17-24 mg eq/kg) demonstrating limited translocation from treated leaves to other plant parts.

The majority of ^{14}C residues in leaves (outer + head) were associated with surface rinses (acetonitrile/H_2O rinse 47–92% TRR). Acetonitrile (rinse + extracts) extracted > 89% of the ^{14}C in leaves (89–98% TRR) and > 23% from roots (23-34% TRR).

Parent pyrifluquinazon and metabolite 1H (IV-01) were the major components observed in all samples of heads and outer leaves. In heads pyrifluquinazon ranged from 3.0-71% TRR (0.026-2.1 mg/kg). In outer leaves, pyrifluquinazon ranged from 65-82% TRR (12-19 mg/kg). Metabolite 1H (IV-01) was detected in heads in the range 13-82% TRR (0.34-1.8 mg eq/kg), and in outer leaves in the range 2.3-21% TRR (0.48-11 mg eq/kg).

In stems a similar pattern was observed, with parent pyrifluquinazon and 1H (IV-01) being the major components of the radioactivity.

Further metabolites were detected at low levels (<10% TRR); 1H-imino (IV-02), 1H-oxide (IV-03), 1H-imino-oxide (IV-04), 1H-4-oxo (IV-15), 1H-N-Ac (IV-17), N-Ac (IV-101), imino (IV-102), quinazolinedione (IV-203) and quinazolinone (IV-206).

PES accounted for 3.8-10% TRR in outer leaves and heads at 14 DALA.

Radish

The metabolism of [^{14}C]- pyrifluquinazon in radish was studied in plants grown in a greenhouse following three foliar applications at seven day intervals of a WG formulation at 0.1 kg ai/ha and at 14 days before harvest.

TRRs were lowest in roots (0.058 to 0.17 mg eq/kg) and the highest in leaves (3.6 to 15 mg eq/kg) demonstrating limited translocation from treated leaves into the roots.

The majority of ^{14}C residues in leaves were associated with surface rinses (acetonitrile/H_2O 50-72% TRR). Extractability of ^{14}C residues with the solvent system (acetonitrile/H_2O, acetonitrile) used was >75% of the ^{14}C in leaves (75-86% TRR) and >36% from roots (36-74% TRR).

Parent pyrifluquinazon was a major component seen in all samples, ranging from 9.2-31% TRR (0.007–0.049 mg/kg) in roots and 49-71% TRR (4.1-8.0 mg/kg) in leaves. The other most abundant metabolite was 1H (IV-01), which was also detected in all samples ranging from 4.1-24% TRR (0.003–0.027 mg eq/kg) in roots and 2.0-18% TRR (0.071-2.7 mg eq/kg) in leaves.

Further metabolites were detected at low levels (<10% TRR); 1H-imino (IV-02), 1H-oxide (IV-03), 1H-imino-oxide (IV-04), 1H-4-oxo (IV-15), quinazolinedione (IV-203), quinazolinone (IV-206) and imino (IV-102).

PES accounted for 57 to 63% TRR in roots of which 8-11% TRR was associated with lignins.

In summary, the metabolism of pyrifluquinazon by plants is well understood and proceeds predominantely through deacetylation of the quinazolinone nitrogen forming 1H (IV-01) and dehydrogenation to imino (IV-102), which may be hydrolysed to the deacetylated metabolite, 1H-imino (IV-02). Trace amounts of 1H-N-Ac (IV- 17) and N-Ac (IV-101) were detected resulting from intra and inter molecular trans-acetylation of pyrifluquinazon. Further transformations of 1H (IV-01) occur via hydroxylation at the 4-position of the quinazoline ring and oxidation at the 1-position of the pyridine ring and N-N bond cleavage.

A number of metabolites were not observed in laboratory animal (rat) studies; these were IV-15 (radish 2% TRR, lettuce 3% TRR, tomato 2% TRR), IV-17 (radish < 1% TRR, lettuce 1% TRR, tomato < 1% TRR), IV-101 (radish, lettuce, tomato < 1% TRR), and IV-102 (radish < 1% TRR, lettuce < 1% TRR, tomato 4% TRR).

Environmental fate

The Meeting received aqueous and soil photolysis, aqueous hydrolysis and aerobic soil metabolism studies for pyrifluquinazon.

The major route of pyrifluquinazon degradation is aerobic soil metabolism. Pyrifluquinazon degraded with a half-life of less than 2 days in laboratory studies on three soils and less than 6 days on additional soils tested under aerobic conditions.

Pyrifluquinazon is stable to hydrolysis (aqueous and soil). Hydrolysis of pyrifluquinazon is rapid under basic conditions and slower under acidic conditions, with a half-life ranging from less than 1 day at pH 9, 24 days at pH 7 to 95 days at pH 5.

Photolysis is not a significant route of degradation.

Rotational crop metabolism

Confined rotational crop studies

In a confined rotational crop study with lettuce, radish and wheat, bare sandy loam soil was treated with [^{14}C]-pyrifluquinazon (Pyr- and Qn-labels) at the equivalent of 206 g ai/ha (2× maximum seasonal rate) and crops sown 30, 120 and 360-390 (419-434 for lettuce) days after the soil application.

For the Pyr-label experiments, the TRRs in lettuce head were < 0.01 mg eq/kg at all PBIs. TRR in radish leaves (30 PBI: 0.004 mg eq/kg,) was similar to those in radish roots for the Pyr-label but much higher in foliage (30 PBI: 0.08 mg eq/kg) compared to roots (30 PBI: 0.014 mg eq/kg) for the Qn-label. For wheat commodities TRRs at the different PBIs followed the order 120>30>360/390 days. In wheat straw residues increased for the longer PBIs (Pyr-label 30 PBI: 0.019 mg eq/kg, 360 PBI: 0.038 mg eq/kg; Qn-label 30 PBI: 0.16 mg/kg equiv, 390 PBI: 0.30 mg eq/kg).

Parent pyrifluquinazon was not detected with either radiolabel in any matrix. No single radiolabelled residue from the Pyr-label samples at any interval contributed ≥0.01 mg/kg. Since the TRR for lettuce (immature, mature) and radish (foliage, roots) was < 0.01 mg/kg, there was no further analysis of residues from these Pyr-label samples. Wheat forage, hay, straw, and grain (Pyr-label) were analysed by HPLC but no metabolites at ≥0.01 mg/kg were extractable with acetonitrile/water.

The TRRs were generally low with the highest levels observed in the Qn-label experiment in radish leaves (30 day PBI: 0.08 mg eq/kg), wheat forage (30 day PBI: 0.11 mg eq/kg), wheat hay (30 day PBI: 0.22 mg eq/kg) and wheat straw (390 day PBI: 0.3 mg eq/kg). Parent pyrifluquinazon was not detected with either radiolabel in any matrix. The only metabolites detected above 0.01 mg/kg were: quinazolinedione (IV-203) (radish foliage 0.025–0.034 mg eq/kg; wheat forage/hay/straw 0.010–0.047 mg eq/kg), a conjugate of quinazolinedione (radish foliage 0.013 mg eq/kg; wheat forage 0.022 mg eq/kg; wheat hay up to 0.066 mg eq/kg; wheat straw up to 0.048 mg eq/kg) and 1H-4-oxo (IV-15) (wheat forage 0.020 mg eq/kg). Residues related to pyrifluquinazon are not expected to be significant at PBIs of a year or more.

Field rotational crop studies

In a field rotational crop study the magnitude of pyrifluquinazon and metabolite quinazolinedione (IV-203) was investigated outdoors in succeeding crops following three foliar applications to the primary crop of mustard greens (3× maximum seasonal rate). Follow crops of radish, leaf lettuce and sorghum were planted at PBIs of 13-14, 29-30 and 58-60 days.

Pyrifluquinazon residues were <LOQ (< 0.01 mg/kg) and IV-203 residues were <LOQ (0.01 mg/kg) in lettuce. Residues of metabolite IV-203 in radish roots were in general < 0.01 mg/kg apart from samples at 30d and 58d PBIs where a maximum residue of 0.015 mg/kg was detected. In radish tops IV-203 residues were 0.012–0.16 mg/kg. IV-203 was detected in sorghum forage at 30d and 58d PBIs in the range 0.010–0.014 mg/kg. IV-203 was < 0.01 mg/kg in sorghum grain except at 13d PBI where a single residue of 0.014 mg/kg was observed. IV-203 in sorghum stover was detected at 14d, 30d and 58d PBIs where residues ranged from < 0.01–0.019 mg/kg. The possible presence of conjugates of IV-203 was not investigated.

IV-203 was detected in field rotational crop studies conducted at approximately 3× the maximum seasonal rate.

Animal metabolism

The Meeting received animal metabolism studies on rats, lactating goats and laying hens.

Rats

Metabolism of pyrifluquinazon in rats was evaluated by the WHO Core Assessment Group of the 2019 JMPR. Metabolites identified in rats included IV-01, IV-02, IV-03, IV-04, IV-27, IV-203, IV206, IV-208, IV-211, IV-303, IV-403, IV-404 and IV-405.

Lactating goats

Lactating goats were orally dosed by gavage once daily for five consecutive days with [^{14}C]-pyrifluquinazon at a dose equivalent to 12 ppm in the diet for the Pyr-label or 11 ppm in the diet for the Qn-label.

By 22 hours after the last dose, the majority of the ^{14}C residues were recovered in the excreta (Pyr-label; urine 12% AD, faeces 45% AD: Qn-label; urine 14% AD, faeces 55% AD).

For tissues, ^{14}C residues were highest in liver (14 Pyr-label, 5.4 Qn-label mg eq/kg) and kidney (2.5 Pyr-label, 0.81 Qn-label mg eq/kg) with lower levels in fat (0.31 Pyr-label, 0.23 Qn-label mg eq/kg) and muscle (0.57 Pyr-label, 0.14 Qn-label mg eq/kg) containing low residues.

Residues in milk appeared to reach plateau levels by four days after the start of dosing (0.7 Pyr-label and 2 Qn-label mg eq/kg in milk fat and 0.25 mg eq/kg both labels in skim milk). There were significant differences in ^{14}C levels between milk collected in the morning prior to dosing compared to evening milk, suggesting pyrifluquinazon residues are rapidly eliminated.

Extractability was good with >67% TRR in kidney, liver and muscle samples extracted with acetonitrile and acetonitrile/H_2O (88-95% Pyr-label, >68-85% Qn-label). Extractability of ^{14}C from milk and fat using acetone/hexane, acetone was good with >90% TRR extracted.

Parent pyrifluquinazon was not detected in tissues or milk.

The predominant components in both skim milk and milk fat were 1H-iminooxide (IV-04) (48-80% TRR) and 1H-oxide (IV-03) (1.8-8.4% TRR). Nicotinic acid N-oxide (11-22% TRR) was also present in Pyr-label milk, as was quinazolinedione (IV-203) (8.4-20% TRR) in Qn-label milk. Aminoquinazolinone-N-Ac (IV-208) (3.8% TRR) was only found in Qn-label milk fat. Lipid conjugates of metabolites contributed 2.2 and 28% of the TRR in milk fat (Qn and Pyr labels respectively) and showed similar properties to fatty acids after saponification (17% TRR for Pyr-label).

The main components in Pyr-label liver were nicotinamide (IV-404) (68% TRR), nicotinic acid (IV-403) (1.9% TRR) and glucuronides of 1H (IV-01), 4-oxo (IV-15) and 1H-4-oxo-imino-oxide (IV-04) found in Qn-label liver (sum 15-43% TRR, mostly IV-01). Other residues found in liver consisted of 1H (IV-01), 1H-4-oxo (IV-15), and quinazolinedione (IV-203), which is unique to the Qn-label (8.4% TRR). Qn-label liver also contained a small amount of residue (3.9% TRR), which had properties similar to fatty acids.

The major residues in kidney were similar to those of liver. Nicotinamide (IV-404) (74% TRR) and methyl nicotinamide (IV-405) (4.1% TRR) were the major residues for the Pyr-label. The same glucuronide mixture that was found in liver was also present in kidney (7.2-17% TRR mostly IV-01), as well as 1H (IV-01) (1.3-13% TRR) and 1H-oxide (IV-03) (1.9-10% TRR). Quinazolinedione (IV-203) (31% TRR), and aminoquinazolinone N-Ac (IV-208) (8.0% TRR) were also present as the major residues from the Qn-label. Qn-label kidney also contained a small amount of residue (3.8% TRR) that had properties similar to fatty acids.

In Pyr-label muscle the major residue was nicotinamide (IV-404) (92-94% TRR). Quinazolinedione (IV-203) (51-57% TRR) and aminoquinazolinone-N-Ac (IV-208) (12-15% TRR) were the major residues identified for the Qn-label, along with lower levels of 1H-oxide (IV-03), 1H (IV-01), and 1H-4-oxo (IV-15). Qn-label muscle also contained a small amount of residue (1.5-4.8% TRR), which was hydrolysed to fatty acids.

For fat the major component in the Pyr-label experiment was nicotinamide (IV-404) (46-79% TRR). Lipid conjugates of metabolites contributed to 18-38% of the TRR in fat. Base saponification of these lipid conjugates released residues that showed similar properties to fatty acids. The major components in Qn-label fat were quinazolinedione (IV-203) (53-58% TRR) and aminoquinazolinone-N-Ac (IV-208) (6.1-10% TRR). Compounds tentatively assigned to lipid conjugates of metabolites contributed to 4.1-8.5% of the TRR in fat.

Laying hens

Laying hens were dosed orally, once a day for a total of seven days, with Pyr- or Qn-label pyrifluquinazon at doses equivalent to 14 ppm in the diet. Sacrifice was at 22 hours after the last dose which is longer than commercial feed curfews of 8-12 hours prior to slaughter.

Excretion of pyrifluquinazon was fast, with 63% AD (Pyr-label) and 77% AD (Qn-label) found in the excreta by 22 hours after the last dose.

TRR for the Pyr-label were highest in liver (6.4 mg eq/kg), followed by muscle (1.0 mg eq/kg), fat (0.16 mg eq/kg) and eggs (0.32 mg eq/kg). TRR for the Qn-label were greatest in liver (2.3 mg eq/kg), fat (0.38 mg eq/kg) and muscle (0.30 mg eq/kg) with residues in eggs rising to

1.6 mg eq/kg. Residues in eggs from both labels continued to increase throughout the collection period.

Extractability of ^{14}C with solvents was good at 62-88% for liver (acetonitrile/water, acetonitrile), 82-91% for muscle (acetonitrile/water, acetonitrile), 86-98% for fat (acetone/hexane, acetone) and >43-88% for eggs (acetonitrile/water, acetonitrile).

Parent pyrifluquinazon was not detected in tissues or eggs.

The major components in Pyr-label eggs were nicotinamide (IV-404) (25% TRR) and 1H-4-oxo (IV-15) (3.2% TRR). Other residues in Pyr-label eggs released by treatment with KOH are thought to be associated with fatty acids (27% TRR). Quinazolinedione (IV-203) (35% TRR), and aminoquinazolinone-N-Ac (IV-208) (50% TRR) were the major residues found in Qn-label eggs. Additional quinazolinedione (IV-203) (2.4% TRR) was released after treatment of Qn-label PES with KOH.

The major residues in Pyr-label liver were nicotinamide (IV-404) (82% TRR), and 1H-4-oxo (IV-15) (4.1% TRR). 1H-4-oxo (IV-15) was also found in Qn-label liver (11% TRR) as was quinazolinedione (IV-203) (25% TRR), aminoquinazolinone-N-Ac (IV-208) (15% TRR), and two polar unknowns (3.6 and 4.6% TRR) that were unique to the Qn-label. Treatment of PES with strong base and acid released additional ^{14}C thought to be associated with fatty acids (7.2% TRR).

The major components in Pyr-label breast and thigh muscle was nicotinamide (IV-404) (73-74% TRR). Nicotinic acid (IV-403) was also found in breast muscle (1.5% TRR) but not in thigh muscle. Quinazolinedione (IV-203) (38-48% TRR) and aminoquinazolinone-N-Ac (IV-208) (27-35% TRR) were the major residues identified in the Qn-label muscles.

In Pyr-label fat, nicotinamide (IV-404) (64% TRR) was the major component. Lipid conjugates of metabolites contributed to 17% of the TRR in fat. Base saponification of these lipid conjugates released residues that showed similar properties to fatty acids. The major components in Qn-label fat were quinazolinedione (IV-203) (75% TRR), and aminoquinazolinone-N-Ac (IV-208) (18% TRR).

The metabolism of pyrifluquinazon was similar in plants, livestock, rats, and in the environment. The primary metabolic pathway for pyrifluquinazon involves initial deacetylation at the 1-position of the quinazolinone ring, yielding metabolite IV-01. Subsequent cleavage of the N-N bond yields quinazolinone-ring metabolites (such as IV-206, IV-208, and IV-203) and nicotinic acid (IV-403), a naturally occurring compound that can be incorporated into biosynthetic pathways. Metabolite IV-01 also undergoes oxidation at the 4-position of the quinazolinone ring to yield metabolite IV-15, or at the 1-position of the pyridine ring to yield metabolite IV-03. In addition, dehydrogenation of the amino group in metabolites IV-01 and IV-03 yields the respective 1H-imino metabolites IV-02 (plants and in the environment) and IV-04.

In plants, pyrifluquinazon also undergoes acetyl group disproportionation (intra- and intermolecular trans-acetylation), yielding minor metabolites IV-101 and IV-17.

In livestock, several of the metabolites (primarily IV-01 and IV-15) also form glucuronic acid conjugates, which are major residues in liver and kidney. Further environmental degradation yields IV-15, IV-02, IV-27, and IV-28.

Methods of analysis

The Meeting received information on analytical methods for pyrifluquinazon in plant and animal matrices.

An important consideration for the analysis of pyrifluquinazon and metabolites is that samples must be kept in the frozen state until addition of the extraction solvent. To achieve this samples are generally homogenised in the presence of dry ice.

The methods all involve homogenisation followed by extraction with an organic/aqueous solvent mixture, typically acidified acetonitrile. In plant commodities, pyrifluquinazon and IV-01 (or IV-203 for rotational crops) are the analytes determined while in animal commodities in addition to pyrifluquinazon, IV-01, IV-03, IV-04, IV-15, IV-203 and IV-208 may also be determined. For liver and kidney conjugates of IV-01 and IV-15 are also determined as the method employs a hydrolysis step with β-glucuronidase. Quantification is by LC-MS/MS. The LOQs for plant commodities are typically 0.01–0.05 mg/kg for pyrifluquinazon and IV-01 while for animal commodities they are 0.01 mg/kg for tissues and 0.005 mg/kg for milk for the individual compounds. The Meeting concluded that the presented methods were sufficiently validated and are suitable to measure pyrifluquinazon and metabolites in plant and animal commodities.

A validated multiresidue method was not avaliable to the Meeting.

Stability of pesticide residues in stored analytical samples

The Meeting received information on storage stability of pyrifluquinazon and IV-01 in raw/processed plant commodities.

Storage stability studies showed that pyrifluquinazon is stable for up to 31 to 377 days at -20 °C in crop commodities representative of the high water, at least 158 days for high acid, up to 67 days for high starch, and up to 163 days for high oil commodity groups. There was considerable variability in the demonstrated storage intervals between different commodities.

1H (IV-01) was not stable in cauliflower and tomato but was stable for up to 31 to 377 days at -20 °C in crop commodities (other than cauliflower, tomato) representative of the high water, up to 158 days for high acid, not stable for high starch, and at least 366 days for high oil commodity groups.

The storage stability of degradate IV-203 was also studied and was stable for at least 67 days in radish root, 81 days in lettuce and 93 days in sorghum grain.

The Meeting agreed that the demonstrated storage stability on various representative plant and animal commodities generally covered the residue sample storage intervals used in the field trials considered by the current Meeting.

Definition of the residue

Plant commodities

The metabolism of pyrifluquinazon was similar in the submitted three plant metabolism studies (radish, lettuce, and tomato).

Parent pyrifluquinazon was a major component seen in all samples (radish root 9.2-31% TRR; radish leaves 49-71% TRR; lettuce heads 3.0-71% TRR, lettuce outer leaves 65-82% TRR; tomato fruit 42-72% TRR). IV-01 was also a significant component of the residue in all samples (radish leaves 2.0-18% TRR; radish roots 4.1-24% TRR; lettuce heads 13-82% TRR, lettuce outer leaves 2.3-21% TRR; tomato fruit 2.4-11% TRR).

Further metabolites were detected but at low levels (<10% TRR): 1H-imino (IV-02), 1H-oxide (IV-03), 1H-imino-oxide (IV-04), 1H-4-oxo (IV-15), quinazolinedione (IV-203), quinazolinone (IV-206) and imino (IV-102).

With the exception of IV-203, residues derived from pyrifluquinazon are unlikely to occur in rotational (follow) crops.

Pyrifluquinazon and IV-01 are the most significant residues in all commodities and validated analytical methods are available for their determination. In field trials IV-01 was sometimes present at higher levels than pyrifluquinazon or the only residue detected.

The Meeting decided that the residue definition for compliance with MRLs in plants should be the sum of pyrifluquinazon and IV-01 (expressed as pyrifluquinazon).

In deciding which additional compounds should be included in the residue definition for risk assessment the Meeting considered the likely occurrence of the compounds present at 10% TRR of pyrifluquinazon, or for the sum of pyrifluquinazon and IV-01, and the toxicological properties of the candidates. Compounds considered are IV-01, IV-02 and IV-203.

Metabolite IV-01 is an intermediate in the metabolic pathway leading to the formation of rat metabolites IV-211 and IV-27 that occur at more than 10% in the rat metabolism study. Therefore, the toxicity of IV-01 is considered to be covered by that of pyrifluquinazon. In view of the absence of repeated dose toxicity studies with IV-02 no conclusion could be drawn on the toxicity of this metabolite. For chronic toxicity the TTC approach (Cramer class III) could be applied as a reverse mutation test on bacteria (Ames tests) was negative for this metabolite.

Metabolite IV-203 is an intermediate in the metabolic pathway leading to the formation of rat metabolites IV-211 and IV-303 that occur at more than 10% in the rat metabolism study. Therefore, the toxicity of IV-203 is considered to be covered by that of pyrifluquinazon.

IV-02 was only a significant metabolite in a Qn-label radish root sample at 14 DALA where it represented 20% of the ^{14}C attributed to the sum of pyrifluquinazon and IV-01. However, the absolute level present was only 0.0025 mg eq/kg.

IV-203 is present at low levels in tomato (0.31-4.5% TRR), lettuce (0.04-1.6% TRR), radish leaves (0.27-1.2% TRR) and radish roots (0.37-3.9% TRR). The contribution of IV-203 from rotational crops would be low compared to direct treatment and also in comparison to residues of pyrifluquinazon and IV-01.

The Meeting agreed it was not necessary to include IV-02 and IV-203 in the residue definition and that the residue definition for dietary risk assessment should be the sum of pyrifluquinazon and IV-01 (expressed as pyrifluquinazon).

Animal commodities

Regarding the residue definition for livestock commodities, the metabolism of pyrifluquinazon in lactating goats and laying hens was qualitatively similar. In the hen metabolism study, birds were slaughtered at 21-22 hours after the last dose compared to commercial practice of 8-12 hours after last feeding. Residues of pyrifluquinazon per se were not found in the metabolism or livestock feeding studies. Rather, the predominant residue in the lactating goat and laying hen metabolism studies was nicotinamide IV-404 (goat: muscle 68-74%, fat 46-79%, kidney 74%, liver 68%; hen: eggs 25%, muscle 73-74%, fat 64%, liver 82%). IV-404 is a vitamin and also a precursor to nicotinamide adenine dinucleotide (NAD) and unlikely to be a compound unique to pyrifluquinazon. IV-404 and other related compounds (IV-402, IV-403, IV-405 and nicotinic acid N-oxide) are not suitable for monitoring compliance.

IV-203 is present in milk (8.4% TRR skim milk, 20% TRR milk fat), eggs (32% TRR) and all tissues in the lactating goat (53-58% TRR fat, 51-57% TRR muscle, 31% TRR kidney, 8.4% TRR liver) and laying hen (75% TRR fat, 38-48% TRR muscle, 25% TRR liver) metabolism studies and would be suitable for monitoring compliance. However, in the lactating cow feeding study the only compounds detected in any tissue were IV-01 in liver and kidney and IV-203 in liver, while IV-04 was the only compound detected in milk. IV-01 and its glucuronide conjugates comprised 8.5–44.5% TRR in kidney and liver.

Methods are available for the determination of pyrifluquinazon, IV-01 and IV-203 in tissues. The method includes a β-glucuronidase hydrolysis step for liver and kidney and therefore determines free and conjugated forms of the metabolites in these tissues. Methods are available for the determination of pyrifluquinazon, IV-04 and IV-203 in milk.

The Meeting agreed the residue for compliance monitoring for tissues and eggs should be the sum of IV-01 (free and conjugated) and IV-203 (free and conjugated) (expressed as pyrifluquinazon).

The Meeting agreed the residue definition for compliance monitoring for milk should be IV-04 (expressed as pyrifluquinazon).

In deciding which compounds should be included in the residue definition for risk assessment, the Meeting considered the likely occurrence of the compounds and the toxicological properties of the candidates nicotinamide IV-404, IV-01 (free and conjugated), IV-03, IV-04, IV-15, IV-17, IV-203 and IV-208.

The nicotinamide IV-404 while the predominant residue in all matrices is not toxicologically significant and the contribution to dietary exposure from natural sources is much greater than from pesticide use. The residues related to pyrifluquinazon of significance were (%TRR):

IV-01 (goat: milk 0.4%, fat 0-1.9%, kidney 8.5-29%, liver 17-45%) for kidney and liver includes glucuronide conjugates

IV-03 (goat: milk 2.4-4.5%, muscle 3.1-3.4%, kidney 10%, liver 1.8%; hen liver 1.5%)

IV-04 (goat: milk 50-70%)

IV-15 (goat: kidney 0.1–0.4, liver 4%; hen: eggs 3.2%, liver 4.1-11%)

IV-17 (goat: fat 4.3%)

IV-203 (goat: milk 16%, muscle 51-57%, fat 53-58%, kidney 31%, liver 8.4%; hen: eggs 32%, muscle 38-48%, fat 75%, liver 25%)

IV-208 (milk 2.6%, muscle 12-15%, fat 6.1-10%, kidney 8%, liver 1.7%; hen: eggs 50%, muscle 27%, fat 18%)

The metabolites IV-01, and IV-203 are intermediates in the metabolic pathway leading to the formation of rat metabolites IV-211, IV-27 and/or IV-303 that occur at more than 10% in the rat metabolism study. Therefore, the toxicity of IV-01 and IV-203 is considered to be covered by that of pyrifluquinazon.

In view of the absence of repeated dose toxicity studies with IV-03, IV-04, IV-15, IV-17 and IV-208, no conclusion could be drawn on the toxicity of these metabolites. For the metabolites IV-17 and IV-208 the TTC approach (Cramer class III) could be applied for chronic toxicity, as reverse mutation tests on bacteria (Ames tests) were negative for these substances. For the metabolites IV-03, IV-04 and IV-15 the TTC for genotoxicity could be applied for chronic toxicity.

The predominant residues in milk are IV-04 accounting for over 70% of the residues structurally related to pyrifluquinazon. IV-04 was the only residue detected in milk in the lactating cow feeding study.

IV-203 forms the major proportion (>75%) of the residue related to pyrifluquinazon in goat fat and muscle and chicken fat while for goat kidney, chicken eggs, chicken muscle and chicken liver IV-203 and IV-208 comprise the major proportion (>75%).

In goat liver, IV-01, and IV-203 account for 89% of the pyrifluquinazon related residues. However as noted above, IV-01 and IV-203 out of pyrifluquinazon, IV-01 and IV-203 was detected in liver or kidney in the lactating cow feeding study.

The Meeting applied the TTC approach to assess IV-02, IV-03, IV-04, IV-15, IV-17 and IV-208. To estimate metabolite concentrations the Meeting utilised the highest ratios of metabolite to the sum of pyrifluquinazon and IV-01 observed in the plant metabolism studies at intervals after the last application relevant to the crops considered by the Meeting to derive factors for fruit, root vegetables and potato.

The maximum long-term (daily) exposures were estimated as 0.03 µg/kg bw for IV-02, 0.49 µg/kg bw for IV-17 and 0 µg/kg bw for IV-208, and are all below the TTC of 1.5 µg/kg bw per day for Cramer Class III compounds. The Meeting concluded that IV-02, IV-17 and IV-208 are unlikely to present a public health concern from the uses evaluated by the current Meeting.

However, the maximum long-term (daily) exposures were estimated as 0.022 µg/kg bw for IV-03, 0.0033 µg/kg bw for IV-04 and 0.017 µg/kg bw for IV-15, and are all above the TTC of 0.0025 µg/kg bw per day for compounds that are potential DNA-reactive mutagens and/or carcinogens. Because the Meeting was unable to conclude on the toxicological relevance of the metabolites IV-03, IV-04 and IV-15, the Meeting could not reach a conclusion on a residue definition for dietary risk assessment.

The Meeting recommended the following residue definitions for pyrifluquinazon:

Definition of the residue for compliance with the MRL for plant commodities: sum of *pyrifluquinazon and IV-01 expressed as pyrifluquinazon*.

Definition of the residue for dietary risk assessment for plant commodities: sum of *pyrifluquinazon and IV-01 expressed as pyrifluquinazon.*

Definition of the residue for compliance with the MRL for animal commodities:

Tissues: sum of IV-01 (free and conjugated) and IV-203 (free and conjugated) (expressed as pyrifluquinazon).

Milk: IV-04 (expressed as pyrifluquinazon).

In deciding whether the residue for compliance monitoring is regarded as fat-soluble, the Meeting noted that residues according to the compliance residue definitions were 0.08–0.09 mg/kg in muscle and 0.11–0.13 mg/kg in fat while residues in skim milk were 0.67 mg/kg and in milk fat 1.0 mg/kg. The Meeting considers the residue should not be classified as fat-soluble.

Definition of the residue for dietary risk assessment for animal commodities: *a conclusion could not be reached.*

Results of supervised residue trials on crops

Supervised trials were available for the use of pyrifluquinazon on stone fruit, potatoes, tree nuts and tea.

Product labels were available from Japan and the USA.

In trials on potatoes and tree nuts, parent pyrifluquinazon and 1H (IV-01) were analysed but found at levels below the LOQ (parent, IV-01). In metabolism studies and residue trials on other crops, pyrifluquinazon and 1H (IV-01) are often found at similar levels. The Meeting decided when residues were <LOQ to add the LOQs.

When calculating the sum of pyrifluquinazon and IV-01, values below the LOQ were assumed to be at the LOQ. Examples are shown below

Table 2. Examples for calculating the sum of pyrifluquinazon and IV-01

Pyrifluquinazon (mg/kg)	IV-01 (mg/kg)	Sum (mg/kg)
< 0.01	< 0.01	< 0.02
< 0.01	0.02	< 0.03
0.02	0.02	0.04

Stone fruit

The GAP for pyrifluquinazon on stone fruit in the USA is applications at 39-53 g ai/ha with a minimum interval between sprays of 7 days, a maximum annual rate of 78 g ai/ha and a PHI of 7 days. The Meeting considered critical GAP to be two sprays, the first at 25 g ai/ha and the second at 53 g ai/ha.

No trials on cherries or peaches from the USA matched critical GAP for the USA.

In seven trials on plums conducted in the USA, at exaggerated rates compared to critical GAP in the USA, where three applications were made at 50 g ai/ha at 7 day intervals, residues at harvest 7 days after the last application were: < 0.02 (6) mg/kg. In some trials, residues were above the LOD but below the LOQ.

The Meeting estimated a maximum residue level of 0.02* mg/kg, a STMR of 0.02 mg/kg and a HR of 0.02 mg/kg for pyrifluquinazon (total) in the sub-group plums.

Tuberous and corm vegetables

In the USA, critical GAP for pyrifluquinazon on tuberous and corm vegetables is 2×53 g ai/ha with a minimum interval between sprays of 14 days, a maximum annual rate of 105 g ai/ha and a PHI of 14 days.

In fifteen trials on potatoes from the USA conducted at exaggerated rates (3×100 g ai/ha at 14 day intervals) residues at harvest 14 days after the last application were: < 0.02 (15) mg/kg.

In storage stability trials on potato, IV-01 levels declined such that only 64% remained after one month of freezer storage and thereafter was relatively stable with 55 to 69% remaining at freezer storage intervals up to one year. The Meeting agreed that considering the exaggerated application rate in the residue trials and a potential decline of residues by 31 to 45%, it can be concluded that residues of IV-01 would have been detected if present and that residues of IV-01 above the LOQ are not expected in trials conducted according to GAP.

Potatoes are a representative commodity for the subgroup tuberous and corm vegetables and the Meeting estimated a maximum residue level of 0.02* mg/kg, a STMR of 0.02 mg/kg and a HR of 0.02 mg/kg for pyrifluquinazon (total) in the subgroup tuberous and corn vegetables based on data for potatoes.

Tree nuts

The Meeting received supervised residue trials conducted in the USA on tree nuts. The GAP for pyrifluquinazon on tree nuts in the USA is applications at 39-53 g ai/ha with a minimum interval between sprays of 7 days, a maximum annual rate of 78 g ai/ha and a PHI of 7 days. The Meeting considered critical GAP to be two sprays, the first at 25 g ai/ha and the second at 53 g ai/ha.

In five trials on almonds and five trials on pecans conducted at exaggerated rates (3×100 g ai/ha at 7 day intervals) residues at harvest 7 days after the last application were: < 0.02 (10) mg/kg. In some trials, residues were above the LOD but below the LOQ.

Almond and pecans are representative crops for tree nuts and the Meeting estimated a maximum residue level of 0.02* mg/kg, an STMR of 0.02 mg/kg and an HR of 0.02 mg/kg for pyrifluquinazon (total) in tree nuts.

Tea, Green, Black (black, fermented and dried)

The Meeting received supervised residue trials conducted in Japan on green tea. In Japan, critical GAP for pyrifluquinazon on tea is 10 g ai/hL with a PHI of 7 days. In six trials approximating cGAP in Japan, residues in green tea (dry) were: 1.2, 2.5, 5.1, 5.7, 6.1 and 14 mg/kg.

The Meeting estimated a maximum residue level of 30 mg/kg and a STMR of 5.4 mg/kg for pyrifluquinazon (total) in tea green, black (black, fermented and dried).

Residues in animal feeds

Almond hulls.

The Meeting received supervised residue trials on almonds. The GAP for pyrifluquinazon on tree nuts in the USA is applications at 39-53 g ai/ha with a minimum interval between sprays of 7 days, a

maximum annual rate of 78 g ai/ha and a PHI of 7 days. The Meeting considered critical GAP to be two sprays, the first at 25 g ai/ha and the second at 53 g ai/ha.

None of the trials matched critical GAP.

Fate of residues during processing

The Meeting received information on the fate of pyrifluquinazon residues during processing in plums, potatoes and infusions of green tea. For potatoes no residues were detected in the RAC or processed commodities. No hydrolysis study simulating processing was made available to the Meeting.

Table 3 Estimated processing factors for the commodities considered at this Meeting are summarized below (residues are for total pyrifluquinazon).

Processed commodity	Raw commodity [STMR/HR]	Individual processing factors	Mean or best estimate processing factor	STMR-P = $STMR_{RAC}$ × PF (mg/kg)	HR-P = HR_{RAC} × PF (mg/kg)
Prune	0.02	1.5	1.5	0.03	0.03
Green tea infusion	5.4	0.0018 0.0026	0.0022	0.012	

Using the estimated maximum residue level of 0.02* mg/kg for plums and applying the processing factor of 1.5, the Meeting estimated a maximum residue level of 0.03 mg/kg for pyrifluquinazon (total) in prunes.

Residues in animal commodities

Farm animal feeding studies

The Meeting received information on the residue levels in tissues and milk of dairy cows dosed with pyrifluquinazon at the equivalent of 0.5, 1.5 and 5.1 ppm in the feed for 28 consecutive days.

In milk, residues of pyrifluquinazon, IV-04 and IV-203 were measured. No residues of pyrifluquinazon or IV-203 above the LOQ of 0.005 mg/kg were detected in any sample. In the 5.1 ppm group residues of IV-04 were detected between 0.005 and 0.008 mg/kg. No residues of pyrifluquinazon or IV-04 or IV-203 were detected in skim milk above the LOQ. In cream samples all residues were < LOQ, apart from the day 13 and 28 samples of cream in the highest treatment group (5.1 ppm diet), which were detected at 0.005 mg/kg.

In tissues, residues of pyrifluquinazon, IV-01, IV-03, IV-15, IV-203 and IV-208 were measured. The only residues detected were IV-01 in liver, at mean levels of < 0.011 (max 0.013), 0.026 (max 0.034) and 0.062 (max 0.074) mg/kg for the 0.5, 1.5 and 5.1 ppm dose groups respectively, IV-01 in kidney of the 5.1 ppm dose group at a mean level of < 0.01 (max 0.01) mg/kg and IV-203 in liver of the 5.1 ppm dose group at a mean level of 0.011 (max 0.013) mg/kg.

A laying hens transfer study was not made available to the Meeting.

Farm animal dietary burden

Potato processing waste was used in estimating livestock dietary burdens.

Dietary burdens were calculated for beef cattle, dairy cattle, broilers and laying poultry based on feed items evaluated by the current Meeting. As there were no feed items relevant to poultry, dietary burdens for poultry are not calculated. The dietary burdens, estimated using the OECD diets listed in Appendix IX of the 2016 edition of the FAO manual, are presented in Annex 6 and summarized below.

Table 4 Estimated maximum and mean dietary burdens of farm animals

	Animal dietary burden: pyrifluquinazon (total), ppm of dry matter diet							
	US-Canada		EU		Australia		Japan	
	max	Mean	max	Mean	max	Mean	max	Mean
Beef cattle	0.08	0.08	0.0967❶	0.0967❸	0.0183	0.0183		
Dairy cattle	0.027	0.027	0.08❷	0.08❹	0.01	0.01		

❶ Highest maximum beef or dairy cattle dietary burden suitable for MRL estimates for mammalian tissues

❷ Highest maximum dairy cattle dietary burden suitable for MRL estimates for mammalian milk

❸Highest mean beef or dairy cattle dietary burden suitable for STMR estimates for mammalian tissues.

❹ Highest mean dairy cattle dietary burden suitable for STMR estimates for milk.

Animal commodity maximum residue levels

Cattle

The calculations used to estimate highest total residues for use in estimating maximum residue levels are shown below.

Table 5 Calculations used to estimate highest total residues for use in estimating maximum residue levels

	Feed Level (ppm) for milk residues	Total residues (mg equiv/kg) in milk	Feed Level (ppm) for tissue residues	Total residues (mg equiv/kg)			
				Muscle	Liver	Kidney	Fat
Highest residue determination (beef or dairy cattle)							
Feeding Study	0.5	< 0.005	0.5	< 0.03	< 0.03	< 0.03	< 0.03
Dietary burden and estimate of highest residue	0.08	< 0.005	0.0967	< 0.03	< 0.03	< 0.03	< 0.03

The Meeting estimated the following maximum residue levels: milk 0.005(*) mg/kg; meat (mammalian except marine mammals) 0.03* mg/kg, mammalian fat (except milk fat) 0.03* mg/kg and edible offal 0.03(*) mg/kg.

No feed items relevant to poultry were considered by the current Meeting and therefore there was no dietary burden for poultry. The Meeting estimated the following maximum residue levels for poultry commodities: eggs, poultry meat, poultry edible offal and poultry fat 0.03(*) mg/kg.

RECOMMENDATIONS

The Meeting concluded on the following residue definitions.

Definition of the residue for compliance with the MRL and dietary risk assessment for plant commodities: sum of pyrifluquinazon and 1,2,3,4-tetrahydro-3-[(3-pyridylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2-one (IV-01) expressed as pyrifluquinazon.

Definition of the residue for compliance with the MRL for animal commodities:

Tissues: sum of 1,2,3,4-tetrahydro-3-[(3-pyridylmethyl)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2-one (IV-01) and 1,2,3,4-tetrahydro-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2,4-dione (IV-203) and their conjugates (expressed as pyrifluquinazon)

Milk: 1,2,3,4-tetrahydro-3-[3-(1-oxy-pyridylmethylene)amino]-6-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]quinazolin-2-one (IV-04) (expressed as pyrifluquinazon).

The residue is not fat-soluble.

Definition of the residue for dietary risk assessment for animal commodities: *a conclusion could not be reached.*

Desirable

Data to clarify potential for residues of IV-203 and its conjugates in rotational Brassica leafy vegetable and cereal (forages, fodder, grain) crops.

DIETARY RISK ASSESSMENT

Because the Meeting was unable to conclude on the toxicological relevance of the metabolites IV-03, IV-04 and IV-15, the Meeting could not reach a conclusion on a residue definition for dietary risk assessment.

As a result long-term and acute dietary risk assessments could not be conducted.

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